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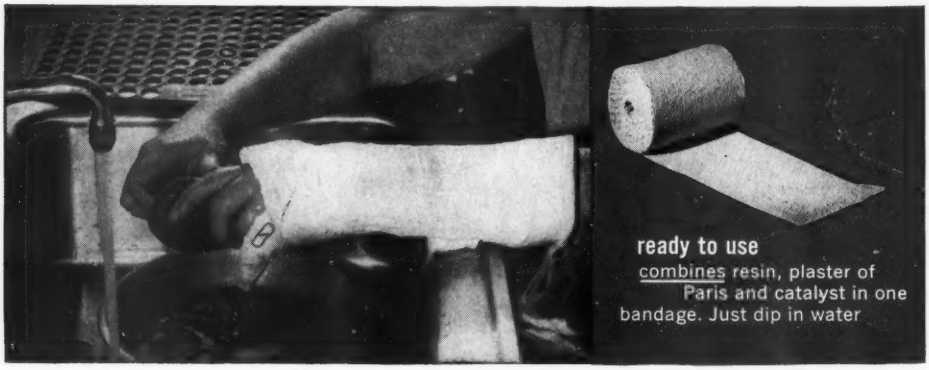

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SURGERY
GYNECOLOGY AND OBSTETRICS

VOLUME 99 DECEMBER, 1954 NUMBER 6

TOTAL GASTRECTOMY FOR GASTRIC CANCER: EFFECT UPON MORTALITY, MORBIDITY, AND CURABILITY

SAMUEL F. MARSHALL, M.D., F.A.C.S., and HERBERT URAM, M.D., Boston, Massachusetts

TOTAL gastrectomy has been advocated in many reports which have been published over the past 10 years, and in many of the more recent reports the mortality rate has very closely approached the operative risk associated with partial gastrectomy. Improvements in modern surgery have brought total gastrectomy within the limits of a reasonable operative mortality rate, and no doubt this mortality rate will further improve with experience in this field of radical surgery. Stone has pointed out that better anesthesia, better control of infection, better knowledge of the physiology of respiration, of the heart and blood vessels, the body chemistry and blood replacement, and many of the factors of preoperative and postoperative care have contributed greatly to the safety of this more radical type of surgical intervention. He warned, however, that the limitations of such operations as well as the possibilities of this new radical surgery of malignant disease must be carefully studied before its proper place in the treatment of malignant disease can be evaluated. This is particularly true of cancer of the stomach. The mere fact that the operative mortality of total removal of the stomach has become low does not justify its routine employment unless a higher rate of curability and prolongation of life can be expected in a larger number of patients; also, the complexity of the problems of the patient after total removal of the stomach must not be overlooked.

From the Department of Surgery, The Lahey Clinic, Boston.

In 1929, Finney and Rienhoff reported a collected series of 67 cases of total gastrectomy, with a mortality rate of 53.8 per cent. Since that time there have been numerous reports on total gastrectomy with a much lower mortality rate, many below 10 per cent. Lefevre and Lortat-Jacob reported 996 cases collected from the literature by 34 authors, and gave an average mortality figure of 29 per cent. Total gastrectomy can be accomplished technically with reasonable operative risk in the hands of experienced surgeons. Does this mean, however, that all patients with carcinoma of the stomach should have a total gastrectomy, or should we consider the other factors that influence not only the mortality but the morbidity and the curability rate? Lahey (16), in an editorial in 1950, raised the question of whether all patients with operable cancer of the stomach should have a total gastrectomy. He emphasized the necessity of a more aggressive approach to this problem of gastric cancer but said that it was not the purpose of the editorial to suggest that every patient with cancer of the stomach should have a total gastrectomy. He emphasized that it would take considerable courage and discrimination on the part of the surgeon to apply such a principle to the surgical treatment of gastric cancer. Allen, in a similar editorial in 1951, agreed that total gastrec-

tomy might be utilized in those patients whose obvious disease process could not be extirpated otherwise, that this should be the operation of choice more frequently than it has been in the past, but he cautioned that it did not appear logical at that time to subject all patients with resectable cancer to a total gastrectomy.

EARLY DIAGNOSIS

It has become more apparent that many factors other than radical surgery influence the curability of carcinoma of the stomach. These include not only early diagnosis and the type of operation but, as MacDonald (21) has pointed out, the final outcome in a case of carcinoma of the stomach is governed by the type of growth rather than by the time or kind of operation. Some tumors grow so rapidly without symptoms that the disease is widespread before the diagnosis is even suspected. The biologic activity of the tumor has much to do with its cure rate. MacDonald further noted that patients whose stomach symptoms are well defined and have continued for some time have a greater chance of a more favorable outcome following surgical intervention.

The onset of gastric carcinoma is often insidious and the early symptoms are too often easily controlled by medication or diet. The physician must be constantly suspicious of the possibility of carcinoma in its early stages, and to do this he must be aware of its frequency, particularly in individuals past the age of 45 years. Epigastric distress, anorexia, nausea, and indigestion do not ordinarily arise without cause and should be thoroughly investigated. We frankly believe that any improvement in the curability of cancer of the stomach depends upon two factors other than radical surgery. First, we must consider the earlier recognition of gastric lesions based upon the alertness of the physician and emphasizing the importance of the educational program not only to the physicians but to the general public. Second, the factor of prevention of gastric cancer has not been explored or even emphasized because the etiology is still unknown.

PRECURSORS OF CANCER

Great progress will be made in the direction of earlier diagnosis when the importance of the precursors, or the premalignant lesions of the stomach, are well recognized. These are, in main, certain types of chronic gastritis; the benign chronic ulcer or any area of the stomach in which ulceration may occur should be regarded as possible premalignant lesions. Polyps (Fig. 1) should be regarded as premalignant lesions; in our experience 35 per cent of gastric polyps have proved to be malignant upon microscopic examination. Henschen has reported a decrease in gastric carcinoma over the last 35 years in the Swedish population and he believes that this decrease is related to the prevention and treatment of the precancerous lesion. It is his opinion that great emphasis should be placed on the possibility that these presumably precancerous lesions may become malignant. Warren and Meissner (41) have stressed that epithelioid and exudative changes occur in association with chronic gastritis which are possibly precancerous in character. The exudative changes, which are evidenced by infiltration of mucosa and submucosa with inflammatory cells, are commonly seen and may progress to intense infiltration with formation of lymphoid follicles in the submucosa. Epithelial changes, which are of more importance, consist of alterations in mucosal cells from the normal which may be progressive, and frequently mitotic figures are formed. Such epithelial changes may be comparable to precancerous lesions noted in other organs.

We should not hesitate to advise exploratory laparotomies in patients in whom alterations in the stomach are noted in the roentgenogram, and possibly more frequently in those patients whose stomach defects are attributed to gastritis as discovered by gastroscopic examination. We should be very suspicious of cancer in the so-called benign gastric ulcer. Clinical evidence seems to support the conclusion that approximately 10 to 15 per cent of the ulcers that appear benign grossly on roentgenologic and clinical examination prove to be malignant on microscopic examination. The diagnosis of carcinoma arising in the benign chronic ulcer must be made with extreme caution pathologically, and only when clinical and radiologic impressions are consistent with the pathologic changes. Meiss-

ner (24) suggested that it is probable that many gastric carcinomas are superficial, particularly in the early stages, and may undergo central peptic ulceration, thus giving a pathologic picture of both ulcer and cancer. In a consecutive group of 411 patients with gastric ulcers who were operated on in this clinic, many of whom came to surgery because cancer could not be excluded by roentgenologic examination, the ulcer proved to be malignant in 65, or 15.8 per cent. It is important, therefore, to remove all gastric ulcers as potentially malignant lesions if they fail to heal (with conservative medical treatment or if they recur after healing is obtained). As Finsterer (8) has pointed out, resection of a gastric ulcer may be regarded as an early operation for cancer of the stomach.

We should be suspicious of a patient with a familial history of gastric carcinoma and it is necessary to carry out thorough laboratory tests on patients with gastric distress and those known to have had an achlorhydria of several years standing. The increased incidence of carcinoma of the stomach in patients with pernicious anemia has been shown repeatedly in reports in the literature. Rigler and Kaplan in 1945 stated that predisposition of patients with pernicious anemia to gastric cancer is three times as great as that of a similar age group without pernicious anemia. Mosbech and Videbaek reviewed records of 301 patients with pernicious anemia and noted 14 deaths from gastric carcinoma, which is three times the expected death rate from gastric carcinoma in patients without anemia. Debray and associates believe that the incidence of gastric carcinoma is much higher in patients with pernicious anemia than in the entire population. They stressed the diagnostic importance of gastroscopy in patients with pernicious anemia. They found 5 gastric polyps in 41 patients with pernicious anemia and 3 of these polyps which were negative to roentgenologic examination were found on gastroscopic examination.

Fig. 1. Total resection for multiple polyps. Microscopic examination showed focus of carcinoma simplex in one polyp.

AGE AND SEX

Gastric carcinoma arises in persons in all walks of life and affects both sexes, with the higher incidence in the male. In this group of 202 total gastrectomies, 184 were for malignant neoplasms, and 61.4 per cent of the patients were males (Table I). This very closely parallels the figures given by the Bureau of Vital Statistics in the United States for 1948, in which 62 per cent of deaths from gastric cancer were reported to occur among males. In the mortality statistics (Table II) from the Metropolitan Life Insurance Company for 1950 and 1951, 68.2 per cent were males and 31.8 per cent were females. The age of the patient may be of some importance in arousing suspicion as carcinoma of the stomach rarely occurs in patients under the age of 45 years. In the Vital Statistics of the United States Government for 1948, 94.5 per cent of patients with gastric cancers were over the age of 45 years. The mortality statistics from the Metropolitan Life Insurance Company give a similar higher incidence in patients over the age of 45; the number of gastric cancers per 100,000 rises rapidly in patients after the age of 45 (Table II). In this group of 184 cases of total gastrectomy for malignant disease, 93 per cent were over the age of 41.

TABLE I.—AGE AND SEX DISTRIBUTION IN 184 CASES

Age, years	No. of cases	Per cent
20–30	2	
31–40	11	
41–50	34	
51–60	67	
61–70	51	
71–80	18	
81–90	1	
Male	113	61.4
Female	71	38.6

171 patients (93 per cent) over 41 years of age.

SYMPTOMS

Physicians must constantly be aware of the possibility of gastric carcinoma in all patients who have persistent gastric distress, and they must be prepared to recognize it in its earliest stages. Epigastric pain and discomfort, anorexia and nausea are among the earliest symptoms; epigastric discomfort or pain is a very common early symptom and was noted in most of our cases. Weight loss, anemia, vomiting, and hematemesis or melena are evidences of advanced carcinoma and, too often, are late manifestations of the disease. The physician should constantly be suspicious of symptoms of indigestion beginning later in life in an individual heretofore healthy, particularly in the male past the age of 45 years, and, therefore, careful laboratory investigation should be carried out at once. Treatment in the form of diet and palliative medicine should not be employed until such studies are obtained. Furthermore, these studies should be repeated if the laboratory findings are negative, particularly when digestive distress persists. The first symptoms noted in this group of 184 cases of gastric cancer are noted in Table III. Epigastric discomfort or pain with anorexia is one of the commonest early symptoms to be noted and such symptoms necessitate roentgenologic and laboratory studies.

Unfortunately, it is true that delay in treatment is often due to the physician or to procrastination on the part of the patient. In a group of 184 cases (170 of carcinoma; 14 of sarcoma) in which total gastrectomy was done, delay in treatment was ascribed to the physician in 70 cases, and to procrastination on the part of the patient in 59 cases. Symptoms of less than 3 months were noted in only 55 patients before they came for treatment. It was noted also that treatment was delayed in a great number of cases (202 cases—benign 18, carcinoma 170, sarcoma 14) because of an erroneous diagnosis by the physician. Forty patients in this group were treated for peptic ulcer without roentgenologic examination or other special laboratory studies being obtained. Fifteen patients of the group had anemia, and no effort had been made to determine its cause. It is a sad commentary that 54 patients out of the group of 184 patients with gastric cancer had had symptoms for more than 12 months before a definite diagnosis was made. It is obvious, therefore, that there is considerable room for improvement in diagnosis. This delay in diagnosis is attributable to the fact that carcinoma was not even suspected, and thus appropriate studies were not carried out early. Any individual who has had symptoms for 3 months or longer before appropriate studies were suggested and obtained has lost valuable time; there were 129 such cases in this series.

TABLE II.—MORTALITY FROM MALIGNANT NEOPLASMS BY SEX AND AGE (1950–1951)*

Death rates per 100,000

	Total		Stomach†	
Age, years	Male	Female	Male	Female
Under 45	114.4	90.4	15.0	6.8
45–54	179.6	187.7	21.3	10.3
55–64	495.0	349.3	64.5	26.6
65–74	968.6	654.8	152.6	74.3

*From Metropolitan Life Insurance Company, Industrial Department.
†68.2 per cent males, 31.8 per cent females.

DIAGNOSIS

The most important factor in establishing diagnosis is alertness on the part of the physician who must constantly be aware of the frequency of gastric carcinoma and who must carry out all possible laboratory studies to determine the presence of carcinoma. In our experience, roentgen diagnosis was accurate in 94 per cent of the patients. Guiss, in a collective review of the end results of gastric carcinoma in 2,891 cases, reported that roentgen examination was accurate in 90 per cent of the

cases, and in an additional 5 per cent the roentgenograms showed a gastric abnormality. Other laboratory methods have proved most helpful in questionable cases and should be utilized whenever carcinoma is suspected but not proved by roentgen examination alone. Gastroscopic examination should be employed in cases of gastric ulcer, gastric polyps, and chronic gastritis in order to make a differential diagnosis. Esophagoscopy should be utilized in all patients with carcinomas involving the cardia in order to determine whether extension to the esophagus is present. If the esophagus is involved, an abdominothoracic approach to the lesion will be necessary. Peritoneoscopy and cytologic techniques are of value and, in some cases, may establish the diagnosis when roentgen examination fails to do so. Other laboratory data, such as determination of the gastric acidity and red blood count, may point toward possible gastric cancer. As stated before, we should be suspicious in cases of long-standing achlorhydria; in this group of 184 patients who had total gastrectomy for cancer, achlorhydria was found in 67 and free hydrochloric acid of less than 20 was noted in 32. Acid values were normal in the remaining 85 patients. Anemia was not an outstanding symptom and was noted in only 71 patients; in 42 the hemoglobin was less than 75 per cent, and in 29, erythrocytes numbered less than 4,000,000. Nevertheless, we should be very suspicious in cases of unexplained anemia. Roentgen examination of the stomach as well as gastroscopic examination should be obtained in all such patients, and particularly in those with pernicious anemia in order to rule out the possibility of gastric polyps or gastric carcinoma.

TABLE III.—EARLIEST SYMPTOM NOTED IN 184 INDIVIDUAL CASES

First symptom noted	No. of cases
Epigastric pain or discomfort	107
Anorexia	20
Dysphagia	11
Nausea or vomiting	11
Weight loss	9
Flatulence	8
Bleeding (hematemesis; melena)	7
Anemia	7
Belching	1
Diarrhea	1
Constipation	1
Intolerance to fatty food	1
Total	184

PATHOLOGIC FEATURES

Unfortunately, there is no uniformity in the literature regarding the classification of gastric tumors, and it is difficult to fit the microscopic features of a carcinoma into a classification based on its gross appearance. We believe that the microscopic characteristics of a carcinoma are by no means an index of the biologic activity or of its inherent malignancy. Warren and Meissner have suggested a working classification which is practical but which does not include some tumors rarely encountered, yet is satisfactory for the clinician and pathologist in discussing the various tumors that arise in the stomach:

A. Carcinoma
   1. Carcinoma in polyp
   2. Adenocarcinoma
   3. Carcinoma simplex
   4. Mucinous carcinoma
   5. Adenoacanthoma
B. Sarcoma
   1. Lymphoma
      a. Hodgkin's disease
      b. Reticulum cell sarcoma
      c. Lymphosarcoma
      d. Lymphocytoma
      e. Macrofollicular lymphoma
   2. Leiomyosarcoma

One characteristic feature of malignant tumors is their ability to metastasize to regional lymph nodes. Meissner (25) has pointed out the frequency with which diffuse lymphatic spread takes place and in particular, he noted that perineural lymphatics may be involved, often with little nodal invasion. Such lymphatic spread may extend across the pylorus to the duodenum and above to the proximal line of resection. He also pointed out that malignant tumors of the stomach have the ability to invade blood vessels and thus metastasize in the blood stream. In his series of 100 resected specimens of cancer of the stomach, blood vessel invasion was found in 57 per cent and showed little relationship to the presence or absence of involvement of lymph nodes. In a group of 100 cases which Meissner studied from the viewpoint of lymph node involvement and other invasive charac-

Fig. 2. Carcinoma of cardia of stomach with extension to esophagus. Segment of esophagus was removed at time of total gastrectomy (November 24, 1952). Patient is living.

teristics, he found that lymph node metastases occurred in 72 per cent. Lymph node metastases in this group of total gastrectomies for carcinoma occurred in 116 cases, or 68.2 per cent. Kuyjer has emphasized that cancer always extends beyond the visible and palpable limits of the lesion. He studied specimens of 70 partial and total gastrectomies and of 57 gastric carcinomas arising in the corpus and antrum ventriculae and in the pylorus; 5 showed involvement of both resection lines, 15 showed extension up to the proximal line of resection, and 16 showed extension to the distal line of resection. Of 13 tumors of the cardia and fundus, however, only 2 showed extension up to the proximal line of resection. Zinninger and Collins, in a similar study of 47 cases, showed also that extension occurred to the duodenum and esophagus. On microscopic study of 30 cases in their series of tumors grossly within 5 centimeters of the pylorus, 9 or 30 per cent showed invasion of the duodenum from a few millimeters to several centimeters; this invasion was not recognized grossly. In 6 cases of carcinoma of the cardia, 5 showed invasion of the esophagus.

TABLE IV.—LOCATION OF GASTRIC CARCINOMA AND AVERAGE SURVIVAL

	No. of cases	Average survival, months
Lesser curvature	35	27.3
Greater curvature	13	26.0
Fundus	24	24.5
Media	35	23.1
Prepyloric	16	17.3
Diffuse	41	13.4
Total	164	

Coller and associates studied intramural and extramural lymphatic spread and found that in 23.5 per cent there was microscopic extension to the line of resection when partial gastrectomy was done. They recommended block dissection of all regional lymphatic metastases corresponding to the vascular supply of the stomach, as well as a wider resection of the gastric tumor.

Gutemann demonstrated that 20 per cent of all partially resected stomachs showed carcinoma in the upper line of the resection, and 38 per cent of all carcinomas of the cardia also involved the lower esophagus (Fig. 2). He believed that only small prepyloric cancers could be removed by partial gastrectomy. Eker, in a study of 100 partial and 70 total gastrectomies, noted that examination of the splenic lymph nodes in 46 specimens showed metastases in 21.7 per cent. In infiltrating carcinoma, no less than 47 per cent showed spread to the splenic group, while only 1 of 21 expansive tumors spread to this area. Tumors of the lower part of the stomach, even on the lesser curvature, showed a strong tendency to spread to the splenic lymph nodes. Thirty-two per cent of gastric carcinomas localized in the upper part of the stomach were found to invade the esophagus. It is evident, then, that in any attempts to extirpate cancer, complete excision of regional lymphatic drainage areas is mandatory. With such a high spread of carcinoma to the splenic lymph nodes, regardless of the site of origin of the tumor, it seems important, if a total gastrectomy is not done nor indicated, that a high partial resection be done which would include a resection of the splenic lymph nodes as well as removal of the spleen. Such a high partial resection which includes removal of the spleen and splenic lymph nodes is undoubtedly a better procedure as it insures more complete removal of all lymphatic drainage areas as well as the removal of

all of the omentum between the spleen and the stomach. It must be realized, however, that although there is a high incidence of spread to the duodenum, the esophagus, and to regional lymph nodes, a significant portion of the immediate lymphatic drainage from the stomach occurs into the peripancreatic tissues which are technically inseparable from the pancreas. These lymphatic drainage areas could be removed *in toto* only by adding total pancreatectomy to the radical operative procedure, but we doubt that such a radical procedure would be justified as it would certainly increase the mortality tremendously and in all probability would not improve the curability rate as such a tumor has extended well beyond the scope of any resection. Allen has pointed out that an adequate and radical block dissection of lymphatic and vascular spread is practically impossible. Routine elimination of nodes along the major vessels and omentum has undoubtedly improved the cure rate, but to go farther than this is not technically feasible or desirable.

The location of gastric cancer in the stomach in this series of cases is shown in Table IV. Lymph node involvement is a fairly constant figure. The incidence of lymph node involvement in a group of 406 cases of gastric carcinoma in which partial resection was performed, ranged from 57 per cent to 66.6 per cent. It has been stated that the more highly differentiated carcinomas, such as the adenocarcinoma, do not metastasize early. This has not been our experience. The rate of metastasis in the adenocarcinomas has been as high as in the less differentiated tumors, such as carcinoma simplex. The average survival in months after total resection for the various types of tumor is shown in Table V, and this indicates little variation in the inherent malignancy of each particular type of neoplasm.

SELECTION OF CASES FOR TOTAL GASTRECTOMY

Total gastrectomy should be employed in those cases in which the disease process cannot be removed unless this procedure is carried out. Obviously, total gastrectomy is not necessary for the small lesion which is in the antral area. Kuyjer stressed that the intramural spread of gastric carcinoma is well

Fig. 3. Thoracoabdominal incision; low left thoracotomy incision, resecting the ninth rib, with extension of the incision through the abdominal wall, dividing the costochondral arch.

recognized. It has been suggested by some writers on this subject that microscopic examination of frozen section material from the edges of the distal proximal lines of resection will assist the surgeon in deciding upon the extent of the resection. This may be helpful in a few cases, but microscopic examination of frozen section material from the gastric or duodenal wall may not be too reliable and to be of any value, many sections would have to be examined which would be a time-consuming procedure. If the examination were negative, the results would still be inconclusive. Frozen section examination is valuable in determining malignancy in an ulcer, in lymph nodes or in sections of a resected segment which may be regarded suspiciously from its gross appearance. Too much dependence, then, cannot be placed on such microscopic study of sections of gastric or duodenal wall, and too often is worthless in making a decision

TABLE V.—SURVIVAL ACCORDING TO TYPE OF CARCINOMA

	No. of cases	Average survival, months
Carcinoma simplex	97	21.6
Adenocarcinoma	54	21.0
Mucinous carcinoma	8	14.9
Carcinoma in polyp	3	27.3
Adenoacanthoma	2	34.0
Total	164	

TABLE VI.—ALL RESECTIONS FOR MALIGNANCY OF THE STOMACH, 1944–1953. PERCENTAGE OF TOTAL GASTRECTOMIES

Year	Total No. of cases	Partial resection No.	Total resection	
			No.	Per cent
1944	38	30	8	21.0
1945	54	45	9	16.6
1946	34	26	8	23.5
1947	63	51	12	19.0
1948	43	32	11	25.5
1949	53	36	17	32.0
1950	60	38	22	36.6
1951	47	37	10	21.2
1952	49	37	12	24.4
1953	57	39	18	31.5
Total	498	371	127	

Mortality: Total gastrectomy, 8.7 per cent; partial gastrectomy, 6.7 per cent.

for radical total resection. The extent of this intramural spread may be difficult to recognize by its gross appearance or by palpation, and microscopic examination of a frozen section of tissue from the edges of the resection of the stomach or duodenum or even the esophagus often gives information that will necessitate removal of all of the invaded tissue but, as pointed out previously, is not too reliable, especially if negative. It is our belief that if the tumor is considered resectable by a high partial resection instead of total gastric resection, a very small remnant of the stomach may be left, and this in no way interferes with radical excision of all groups of lymph nodes. Partial or total resection should always include the splenic lymph nodes as well as the removal of the spleen, the greater omentum, and a generous segment of the duodenum above the ampulla of Vater.

It is our conviction that unless the surgeon undertaking surgical treatment of gastric cancer is trained for and experienced in radical resection for gastric cancer such as total gastrectomy, he should not undertake the original laparotomy. The surgeon cannot foretell from the roentgenogram in every case the extent of radical resection that will be necessary. He should be prepared if necessary to extend the abdominal incision into the thoracic cavity (Fig. 3) and should be able to proceed with a radical total removal of the stomach and complete excision of all lymphatic drainage areas. Excision of the pancreas, transverse mesocolon, transverse colon, and left lobe of the liver will be necessary when adherent cancers extend into these organs. Experienced gastric surgeons will not hesitate to employ these procedures if the gastric tumor appears to be resectable and complete extirpation of the cancer may be possible. Although palliative partial gastrectomies are often worth while, we are convinced that palliative total gastric resection should not be attempted. Total gastrectomy should be employed only in those cases in which there is a reasonable chance of removing all carcinomatous tissue. We are in agreement with Welch and Allen (42) that if all gross tumor cannot be removed by total gastrectomy, the best palliative operation is partial gastrectomy. We see no reason to utilize total gastric resection nor would we advocate such a procedure as a routine method of treatment for gastric cancer.

The percentage of total gastric resections employed in all resections for gastric cancer in the Lahey Clinic over the past 10 years is shown in Table VI. The percentage of total resections has ranged between 20 and 30, and it is interesting to note that this percentage has remained fairly constant during this period. Cancers arising in the distal half of the stomach or in the prepyloric region may be radically removed by a high subtotal resection. In all cases the spleen is removed in view of demonstrated metastasis to the splenic nodes in many gastric cancers, the omentum is removed completely, including the omentum between the spleen and the greater curvature, and the gastrohepatic omentum, and a small part (15 to 20 per cent) of the stomach is permitted to remain above. This facilitates the jejunal anastomosis and favorably affects the postoperative feeding problem. Lymph nodes in the pyloric area and about the celiac axis and curvatures of the stomach should be included in the block dissection, and the first part of the duodenum, almost to the common bile duct, should be excised routinely. Removal of all the lymphatic drainage areas is of far greater importance than the benefit ob-

tained from total gastric resection in all cases. Diffuse gastric cancer (Fig. 4), cancers extending high on the lesser curvature, and cancers arising in the cardia demand total gastrectomy. In view of the tendency of carcinoma arising in the cardia to extend into the esophagus, a portion of the esophagus must also be excised. Lymphatic drainage also may involve the peripancreatic region which is technically inseparable from the pancreas and would require a partial or total pancreatectomy. The latter procedure (total) is not justified because of the operative hazard and the scant hope offered to the patient that there will be no further spread of invasive carcinoma beyond the scope of such a radical surgical extirpation.

Fig. 4. Total gastrectomy for diffuse carcinoma simplex of cardia, extending to prepyloric area. Regional lymph nodes were involved. Patient is alive 4 years after operation.

SURGICAL TECHNIQUE

The surgical technique of total gastrectomy as used in the Lahey Clinic has been described in previous studies. Many aspects of this operation are discussed and the different techniques employed are described in many articles in the literature.

Total gastric resection can be accomplished most satisfactorily in the majority of patients through an abdominal incision (Fig. 5). A left transrectus incision extending from the costal margin caudalward to just below the level of the umbilicus is employed. The abdominal cavity can thus be explored and decision made for partial or total gastrectomy. If total gastric resection is required, the incision can be extended and made thoracoabdominal by cutting across the costochondral arch into the fifth or sixth interspace. Incision of the diaphragm can be carried through the hiatus if a portion of the esophagus is excised. Often it is unnecessary to incise the diaphragm as the cardia and lower end of the esophagus can be exposed by merely dividing the costal margins and retracting them, thus making the approach to the lower esophagus immeasurably easier. With division of the vagus nerves and occasionally with division of the crura of the diaphragm, a long segment of the esophagus can be exposed and excised readily. We prefer the abdominal incision with the added division of the costal margins when needed as the complete removal of the lymphatic drainage areas in the abdomen is facilitated through such an incision.

If desired, and if the need for total resection is evident from the roentgenogram and from information obtained of esophageal involvement by esophagoscopy, a thoracoabdominal approach can be made by a low left thoracotomy incision. The ninth rib is resected and the incision through the abdominal wall is extended in the direction of the thoracic incision by cutting the costochondral arch (Fig. 6).

Determination of operability after the abdominal cavity is opened cannot be made by merely palpating the tumor. The abdominal cavity and viscera are carefully explored, and if no metastases are found traction is made on the transverse colon and omentum. The omentum is separated from the transverse colon by incision and the lesser omental cavity is exposed. With the stomach turned upward and with complete detachment of the omentum from the transverse colon, wide exposure of the lesser omental cavity and pancreas is obtained (Fig. 7).

Extension to the pancreas and to the celiac axis and mesocolon can easily be determined and a decision made concerning operability. If the carcinoma proves too extensive for a resection, the operation can be terminated by

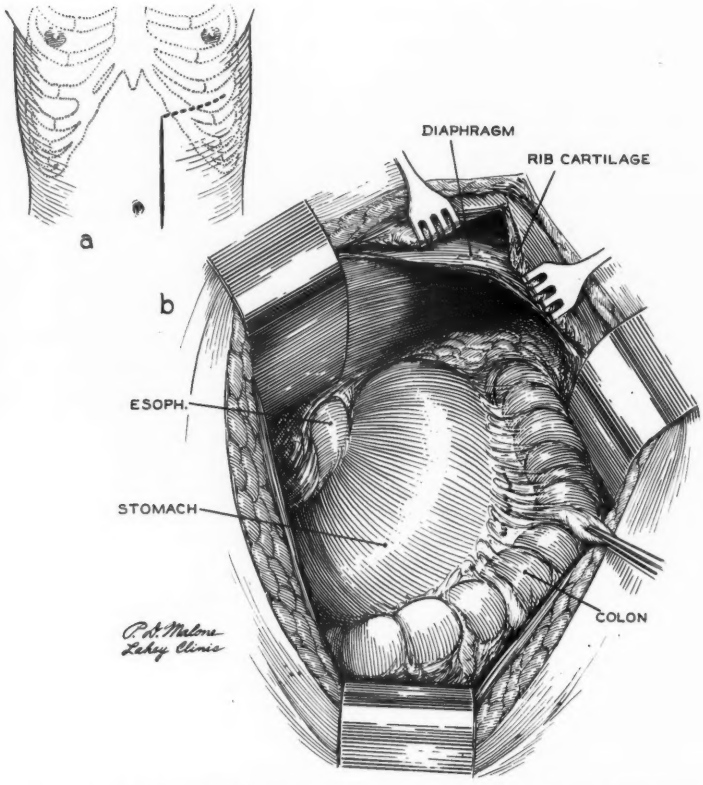


Fig. 5. Type of incision employed in total gastric resection. Insert a, left transrectus incision extending to the costal margin. b, Exploration of tumor and abdominal cavity is made through the abdominal incision; the decision can then be made as to whether total resection of the stomach is necessary to remove the cancer. Better exposure of the cardia and esophagus can be obtained by dividing the costal margin, as indicated by the broken line. Drawing illustrates the exposure obtained by retracting the divided costal margin; if necessary, the diaphragm can be incised, carrying the incision through the hiatus for better exposure of the lower end of the esophagus, opening into the thoracic cavity.

dropping the colon and omentum back into the abdominal cavity and without closure of the lesser omental cavity. If the gastric lesion appears to be resectable, total gastrectomy can be carried out rapidly by mobilizing the pylorus and duodenum, ligating the right gastric and right gastroepiploic vessels, and removing all nodes in this region by block dissection. The duodenum is then transected, the distal segment inverted and closed, and an adequate segment of the first part of the duodenum removed with the stomach turned cephalad. The surgeon then proceeds with ligation of the left gastric artery as it branches from the exposed celiac axis. The peritoneal and loose areolar tissue about the celiac axis is incised to expose the axis and its branches. All nodes in this region can thus be stripped readily. The splenic artery just above the upper border of the pancreas is followed to the splenic hilum, and the splenic artery, together with the splenic vein, is ligated just proximal to the left gastroepiploic artery. This will divide the splenic blood supply and permit re-

moval of the spleen, as well as control the bleeding from the short gastric vessels (Fig. 8). The major blood supply of the stomach is thus controlled easily by ligation of the major vessels. It again should be emphasized that the removal of the spleen, the omentum, and all possible groups of lymph nodes is exceedingly important, and in most instances, can be done more readily through the abdominal or thoracicoabdominal incision than through the transthoracic incision. The type of incision that can be utilized in making a combined incision for the total removal of the stomach is shown in the insert in Figure 5. Gastrointestinal continuity is re-established after total gastrectomy by anastomosis of the end of the esophagus to a loop of the jejunum. This was done in all total gastrectomies with the exception of 2 in which an esophagoduodenostomy was done. An enteroenterostomy is always done (to form a food pouch). This is a simple, effective method and more experience with this simple method has proved that it is quite satisfactory.

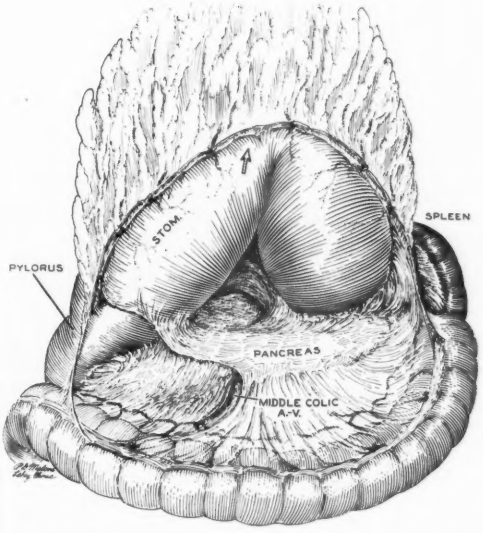


Fig. 6. Lesser omental cavity is exposed by separating the greater omentum from the transverse colon. Stomach is retracted upward. Cancer invasion of the pancreas and about the celiac axis as well as retrogastric extension can readily be seen and resectability determined.

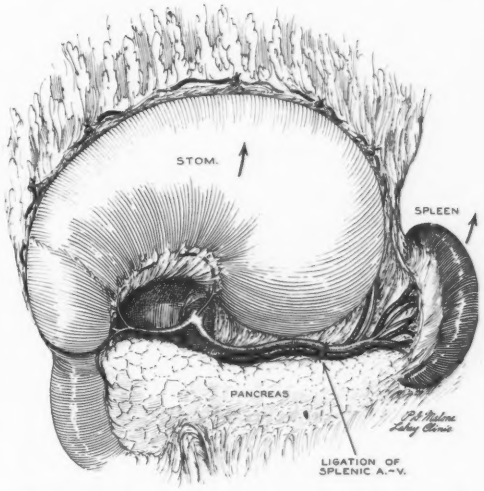


Fig. 7. Blood supply of the celiac axis. Splenic vessels can be ligated just above the pancreas, controlling the blood supply to the spleen and to the greater curvature through the left gastroepiploic vessels. The spleen can then readily be removed with the stomach.

We fail to see the benefits to be gained by the employment of the cecum or portion of the transverse colon in forming a food pouch. These food pouches, regardless of how they are made, act only as a reservoir, have no digestive function and do not serve to increase the comminution or the mixing of food with pancreatic and biliary secretions. A food pouch formed by anastomosis of two loops of the jejunum as an enterostomy has proved adequate in our hands. It is much more easily performed and is accomplished without contamination such as would be associated with utilization of any segment of the colon.

OPERATIVE MORTALITY

The mortality following total gastrectomy during the period from 1927 to 1943 inclusive was 34.6 per cent. Over the past 10 years the postoperative mortality in 127 cases was 8.7 per cent (Table VII). The operative mortality as reported in the literature by numerous authors is shown in Table VIII; in general, the mortality of total gastrectomy decreased over the past 10 years. In the earlier years in our group of 75 cases with 34.6 per cent mortality (26 cases), death in 22 pa-

TABLE VII.—CAUSE OF POSTOPERATIVE DEATH IN 202 TOTAL GASTRECTOMIES

	No. of cases	No. of deaths
Total gastrectomies 1944–1953	127	
Cause of death		
Embolism		1
Cardiovascular disease		6
Peritonitis (sepsis)		4
		11
Total gastrectomies 1927–1943	75	
Cause of death		
Embolism		1
Cardiovascular disease		3
Peritonitis	(sepsis 22)	17
Mediastinitis		2
Pneumonia		3
		26

tients (84.6 per cent) was due to sepsis, which included peritonitis, mediastinitis, and pneumonia. With the employment of chemotherapy and antibiotics, the operative mortality has decreased considerably during the past 10 years, as there were only 4 deaths attributable to sepsis which resulted from contamination. In 1950, Finsterer (9) reported a mortality of 49.5 per cent in 103 cases of total gastrectomy and stated that the chief cause of death aside from infirmities or age was infection of some type. Undoubtedly, many of the deaths resulting from infection might have been prevented by the use of antibiotics.

The various types of total resection of the stomach as done in the Lahey Clinic are shown in Table IX. In this group of 202 total gastrectomies, 20 patients had resection of adjacent viscera. There were 2 deaths, a postoperative mortality of 10 per cent, which is essentially the same as for the entire group of 127 cases (1944 to 1954), i.e., 8.7 per cent. Extending the scope of the operation by resecting adjacent viscera apparently did not appreciably affect operative mortality. In the group of 127 total gastric resections, in addition to 4 deaths from peritonitis, which presumably now could be avoided by prevention of contamination and by use of antibiotics, there were 6 deaths as a result of cardiovascular complications and 1 death attributable to embolism. In the first series of 75 cases, 1 death was attributed to embolism and 3 deaths were ascribed to cardiovascular disease. The prevention of death by control of sepsis is thus quite a factor in postoperative mortality.

There were 2 postoperative deaths in the group of 18 cases with benign lesions in which total gastrectomy was performed. Most of the total gastrectomies in this group of 18 cases were done because the gross appearance of the lesions was that of carcinoma. In 14 of the 18 cases, the ulcers were large, many of which, because of their gross appearance, were inaccurately thought to be carcinoma.

LATE RESULTS

From a study of many reported series of total gastrectomies and from an analysis of this series of 202 cases of total removal of the stomach, it is obvious that these operations can be done with a reasonable degree of safety. We believe that this operative mortality can in time be still further reduced until it approaches the operative risk of partial gastrectomy, which in this clinic is 5.7 per cent. However, other factors must be considered carefully. First, can we improve the curability rate and, second, can we avoid the many postoperative problems, such as control of diet and maintenance of sufficient caloric intake, and achieve a comfortable existence for the patient so that he is able to carry on his normal occupations and maintain a reasonably satisfactory economic status? Will any additional increase in cure rate compensate for these factors of morbidity? Curability is difficult to evaluate since in the great majority of patients total gastrectomy has been done for extensive cancer and the disease process is so diffuse that nothing short of total resection will remove the lesion. We cannot assume that recurrent carcinoma in the gastric stump after partial resection is prima facie evidence that total gastrectomy might have cured the patient. We have no evidence that enough of the stomach was removed or how far beyond the gross tumor the line of transection was made. de Amesti found that 45 per cent of recurrent tumors were located in the gastric stump; these findings were based on roentgenologic and gastroscopic examination alone. McNeer and associates, in a study of 92 autopsy protocols collected from several hospitals in New York, found local recurrence in 56 per cent of survivors; in 30 per cent, the recurrence was located in the gastric stump.

They concluded that 56 per cent of patients were denied a chance of cure because of inadequate surgery. On the other hand, one does not know whether the original partial resection was a thorough and adequate one. Warren reported 23 cases (19.6 per cent) of recurrent carcinoma in the gastric stump in necropsies on 122 patients who died of recurrent disease after partial resection—here again the extent of the partial resection is not known.

In order to evaluate curability of total gastrectomy, it will be necessary to compare the results of large groups of cases of total and partial gastric resection in which the operation was done for comparable lesions and the patients were followed for at least 5 years after operation. Moreover, such an evaluation of results must be based on standard operative procedures for both total and partial resection in order to obtain significant data. Concurrent series of cases of radical high partial resection with excision of the duodenum and spleen and careful block dissection of lymphatic spread should also be studied to arrive at any sound conclusion.

There are very few reports on late results after total gastrectomy. The survival rates in the main are based on advanced and diffuse cancer, and consequently, they cannot be compared with the survival rates following partial gastrectomy. There is a paucity of reports on 3 and 5 year survivals after total gastrectomy. Many of the reports cite isolated cases and in almost all, fewer than 6 patients survived appreciable periods. We have had a 5 year survival rate of 27.3 per cent after partial gastrectomy. Allen stated that 22 per cent of his patients who survived resection were cured; de Amesti reported a 5 year survival of 11 per cent after partial gastrectomy and stated that he has widened his indications for total gastrectomy. Survival rates after total gastrectomy are much lower than after partial gastric resection but, of course, the results of total and of partial gastrectomy cannot be compared, as these operations were not done for comparable lesions.

ReMine and Priestley reported that 17 of 80 patients (21 per cent) who had total gastrectomy for malignant lesions of the stomach survived 3 years and 9 (18 per cent) of 50 patients traced lived 5 years after operation. One of their patients who survived 5 years had had a lymphosarcoma. Finsterer (10) reported 9 patients up to 1946 who survived from 5 to 9½ years after total resection; the 9 cures represent 17.3 per cent of all patients who survived total gastrectomy. Sweet reported a series of 77 cases of gastric carcinoma in which total gastrectomy was performed through the thoracic or abdominothoracic approach, with 15 postoperative deaths (19.5 per cent). He further stated that of 44 pa-

TABLE VIII.—MORTALITY RATES OF TOTAL GASTRECTOMY REPORTED IN LITERATURE

Authors	Year reported	No. of patients	Mortality, per cent
Finney and Rienhoff (collected series)	1929	67	53.8
Walters, Gray, and Priestley (37)	1942	27	66.7
Pack and McNeer (27)	1943	298	37.6
Lahey and Marshall (17)	1944	73	33.3
Pack, McNeer, and Booher (28)	1947	41	31.7
Longmire	1947	20	10.0
Wangensteen	1949	28	3.5
Scott and Longmire	1949	63	9.5
Lahey and Marshall (18)	1950	64	9.4
Lefevre and Lortat-Jacob (collected series—34 authors)	1950	996	29.0
de Amesti	1950	30	13.3
Finsterer (9)	1950	103	49.5
ReMine and Priestley	1952	108	12.9
Walters, Gray, and Priestley (38)	1952	19	5.3
Winkelbauer	1952	32	25.0
Finsterer (10)	1953	150	57.3
Troell	1953	54	51.0
Ransom	1954	43	17.1
Marshall and Uram	1954	127	8.7

TABLE IX.—TYPES OF TOTAL GASTRECTOMY—202 CASES

		No. of cases
A.*	Total gastrectomy with splenectomy and jejunojejunostomy	111
B.	Total gastrectomy with splenectomy	36
C.	Total gastrectomy with jejunojejunostomy	34
D.	Total gastrectomy only	21
	Total	202

*20 patients in Group A had resection of adjacent viscera—colon, pancreas, liver, gallbladder, lower third of esophagus—with 2 deaths.

TABLE X.—SURVIVAL AFTER TOTAL GASTRECTOMY FOR MALIGNANCY IN 184 CASES

	Carcinoma No. of cases	Sarcoma No. of cases	Survived operation No. of cases
Postoperative deaths	34	1	
Survival, years			
Less than 1	53	4	57
1 to 2	38	1	39
2 to 3	14	0	14
3 to 4	11	0	11
4 to 5	4	3	7
5 or more	16	5	21
Total	170	14	149

26.2 per cent lived 3 years or longer.
14.1 per cent lived 5 years or longer.

TABLE XI.—PATIENTS NOW LIVING WITHOUT KNOWN RECURRENCE AFTER TOTAL GASTRECTOMY FOR CANCER

Survival, years	Carcinoma No. of cases	Sarcoma No. of cases	Total now living No. of cases*
Less than 1	12	1	13
1 to 2	7	1	8
2 to 3	5		5
3 to 4	8		8
4 to 5	1	2	3
5 or more	14	5	19
Total	47	9	56 (37.6%)

*Of 149 patients who survived operation.

TABLE XII.—TOTAL GASTRECTOMY FOR CARCINOMA IN 170 CASES

	Lymphatic metastases* 116 cases, 68.2 per cent			No lymphatic metastases† 54 cases, 31.8 per cent		
	Living and well No. of cases	Alive with recurrence No. of cases	Dead No. of cases	Living and well No. of cases	Alive with recurrence No. of cases	Dead No. of cases
Postoperative deaths			19			15
Survival, years						
Less than 1	10	4	31	2	1	5
1–2	4	3	19	3	3	6
2–3	3	2	4	2		3
3–4	3		3	5		
4–5	1		2		1	
5–6	1			1		
6–7	3		1	1		
7–8				1		1
8–9						
9–10	1			2		
10–11						
11–12	1					
12–13				1		
13–14	1					
Total	28	9	79	19	5	30

*18 patients (18.5 per cent) of those who survived operation are alive and well 1 year or more.
†17 patients (43.6 per cent) of those who survived operation are alive and well 1 year or more.

tients on whom total gastrectomy was done more than 3 years ago and who survived, 9 were alive after 3 years (20 per cent) and of 28 whose operation was performed 5 or more years ago, 2 survived 5 years.

In this series, 184 total gastrectomies were performed for malignant tumors; 14 were done for sarcoma and the remainder for carcinoma. Of the 149 patients who survived operation, 39 patients (26.2 per cent) lived 3 years or longer and 21 patients (14.1 per cent) lived 5 years or longer (Table X).

The number of patients still alive without malignant disease after total resection is shown in Table XI. It is interesting to observe that of those having total gastrectomy for cancer, 11 patients are alive and well 5 to 10 years, and 3 are living and well 12 to 14 years after operation (Table XII). There was carcinomatous involvement of regional lymph nodes in 116 (68.2 per cent) of 170 patients. The effect of lymph node involvement upon survival is significant. Of 116 patients with lymph node involvement, 97 survived operation and only 18 patients (18.5 per cent) are living without recurrence 1 year or longer. In sharp contrast, there were 54 patients without regional lymph node invasion, and of the 39 who survived operation 17 (43.6 per cent) are alive and well 1 year or longer after operation (Table XII).

The survival rate after total gastrectomy for sarcoma was much better than for cancer. There were 14 cases of sarcoma, 2 of which were leiomyosarcoma, and there was 1 postoperative death. Five (38 per cent) of 13 patients who survived total resection are alive and well 5 years or longer; 3 patients with

malignant lymphoma are alive and well 11 to 15 years after operation (Table XIII).

The site of origin in cancer of the stomach appears to have very little influence on survival after total resection with the exception of prepyloric lesions and diffuse gastric carcinoma. It is disturbing to note that the average survival of patients with prepyloric cancer, where the best results with total resection might be expected, is definitely less than in other areas and almost as bad as the average survival rate in cases of diffuse gastric involvement (Table IV). It would seem that radical removal of the gastric wall was not nearly as important as removal of all other lymphatic drainage areas. We can draw no definite conclusion regarding survival from the type of malignancy except that mucinous carcinoma has the poorest survival average (Table V) of all types of cancer.

Splenectomy was not done in our earlier group of cases (46) and in this group only 10.9 per cent lived 5 years or more, whereas 14.1 per cent of the entire group of 184 patients with cancer lived 5 years or more.

Splenectomy is a routine procedure now in all total resections of the stomach, and we believe that the spleen should be excised also in all partial gastric resections for cancer in order to remove all possible lymphatic avenues of invasion. Splenectomy is easily accomplished and does not add to the operative mortality.

It is of interest to note that microscopic examination disclosed cancer near or through the line of resection in 20 cases (10.8 per cent). With extension into the duodenum or esophagus, 17 patients who survived operation lived less than 2 years, with 15 patients dead in the first year. It is questionable whether any form of radical resection would have benefited these patients since the tumor had probably invaded elsewhere too.

There were 18 patients with benign lesions who had total gastrectomy; this included 14 patients with benign gastric ulcers, 2 patients with diffuse advanced gastritis, and 2 with large leiomyomas. There were 2 postoperative deaths and 4 patients have died of other disease since operation. Twelve patients are alive and well, the majority with very little postoperative difficulty. Eight of the 12 are alive and relatively well 5 to 10 years after operation.

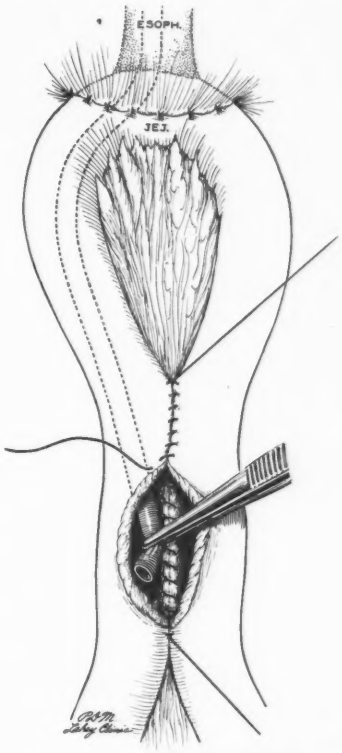


Fig. 8. At completion of esophagojejunostomy the indwelling nasal catheter within the esophagus can be pulled down into the pouch formed by the jejunojejunostomy, thus permitting early introduction of fluids into the jejunum.

We do not believe that there is any convincing evidence as yet that total gastrectomy should be used as a routine method in all cases of gastric cancer but that further intensive study of this problem is urgently needed before any definite conclusion can be stated. Undoubtedly, there is a definite place for the employment of total gastrectomy in gastric cancer, and such cases should be selected with great care. Total gastrectomy can be a very valuable procedure and the gastric surgeon must be prepared to employ such a method when indicated. He must, however, be prepared to accept increased mortality and morbidity.

TABLE XIII.—SURVIVAL AFTER TOTAL GASTRECTOMY FOR SARCOMA IN 14 CASES

	Living and well No. of cases	Alive with recurrence No. of cases	Dead No. of cases
Postoperative deaths			1
Survival, years			
Less than 1	1		3
1 to 2	1		
2 to 3			
3 to 4			
4 to 5	2	1	
5 to 6	1*		
11 to 12	1		
12 to 13	1		
14 to 15	1		
16 to 17	1*		
Total	9 (64.3%)	1	4

*Leiomyosarcoma.

POSTOPERATIVE COURSE

Many problems arise from altered nutrition after total removal of the stomach. Allen raised the question as to whether total gastrectomy would increase the curability sufficiently to offset the consequent morbidity. He believed that if the patients survive a sufficient number of years they can usually adapt themselves to the absence of the entire stomach. There are very few studies on the postoperative course of patients who have survived varying periods after total gastrectomy, but the number of survivors is as yet too small, and accurate data in a sufficient number of cases are too limited. It is also obvious that many individual variations of postoperative difficulties will arise and those problems must be considered as they occur.

Feeding can be started very early after total gastrectomy, usually after the second day. This can be done through an indwelling nasal catheter which is drawn down through the esophagojejunal anastomosis and the lower end placed in the newly formed food pouch (Fig. 8). Fluids and gastrostomy feeding can gradually be increased and given through this tube; nothing is given by mouth for the first 5 or 6 days.

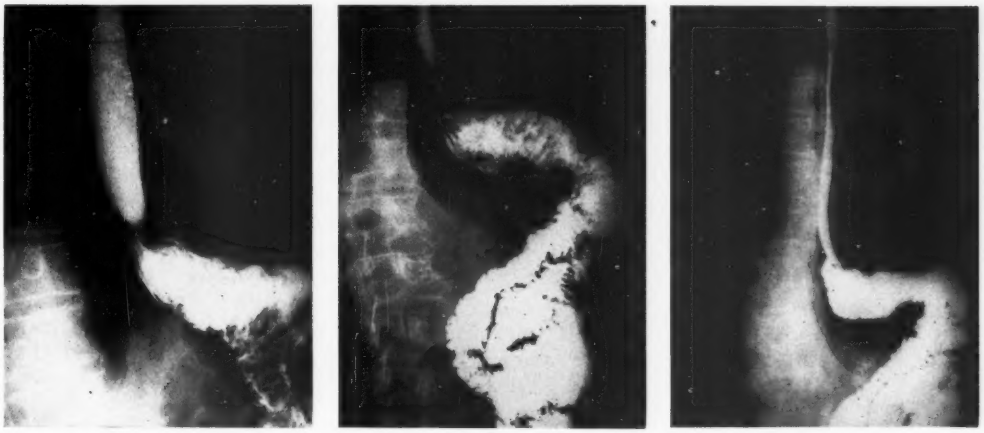
Epigastric and substernal burning and distress were not uncommon occurrences in our earlier cases before jejunojejunostomy was performed. This enteroenterostomy acts to deflect the bile, duodenal, and pancreatic secretion away from the anastomosis, thus relieving distress, and if a sufficiently long segment of the jejunum is used for the anastomosis the pouch formed becomes a very satisfactory reservoir for food.

Nutrition does present a problem after total gastrectomy. We doubt whether any patient will ever become obese after the removal of the entire stomach, and many patients find it difficult to gain or even to maintain weight. Of this group who survived total gastrectomy, 10 individuals maintained normal weight and 11 gained from 2 to 20 pounds. The general trend, however, was a marked loss of weight in the majority of cases. Everson has pointed out that there is impaired assimilation of fat and also of protein food. In only 3 of 40 cases that he collected was weight following total gastrectomy restored to the normal preoperative level. Likewise, experimental animals either lost, or failed to gain weight following total gastrectomy when they were fed diets just sufficient to maintain weight in normal animals. He concluded that a high caloric, high fat, high protein, low carbohydrate diet taken in the form of numerous small meals should be recommended after total gastrectomy in order to maintain an optimal nutritional status, and this caloric intake should be much higher than would be sufficient to maintain weight in a normal individual with a normal stomach. ReMine and Priestley reported that about two-thirds of 13 patients who survived total gastrectomy 5 years or more regained their preoperative weight and that the remainder were unable to do so.

From evidence available it would seem that carbohydrates are well assimilated after total gastrectomy but a low carbohydrate diet is advised because the dumping syndrome is likely to arise when large amounts of carbohydrates are used.

Everson recommended a high caloric diet, 50 or more calories per kilogram of body weight, taken in frequent small feedings for maintenance of nutritional status.

The dumping syndrome, as evidenced by symptoms of excessive fullness, weakness,



a b c

Fig. 9. Total resection of gastric carcinoma, February 13, 1948. a, Esophagojejunal stenosis September 13, 1948; b, after dilatation; c, esophagojejunal anastomosis March 24, 1953. No obstruction was present. Patient is alive and well more than 6 years after operation.

sweating, nausea, and palpitation, can be avoided to a large degree with frequent small meals and limitation of fluids at the time of meals. Anticholinergic drugs, such as atropine sulfate, banthine, and similar drugs, reduce intestinal motility and may prevent fecal fat and nitrogen loss after total gastrectomy, but these drugs also have an inhibitive effect on pancreatic secretion.

Smith, in following a group of our cases after total resection, stated that it is impossible to overemphasize the importance of constant supervision of diet and nutrition after total gastrectomy; in this we agree and we believe that many of the digestive difficulties could be avoided or controlled by such management. Because of loss of the macerating and mixing functions of the stomach, the patient must be instructed to eat slowly and chew food carefully. Those patients who have poor teeth should have food finely divided and should avoid roughage so that the food is not too irritating to the jejunum. Ingelfinger believed that some of the symptoms arising after total gastrectomy have actually been caused by jejunitis. Zollinger and Ellison stated that it is the responsibility of the surgeon to insure good nutritional status after gastric surgery, and this is especially true after total gastrectomy. In this clinic, the surgeon enlists the help of the gastroenterologist in very carefully supervising these patients after operation, and the patient's course is followed at regular intervals. When nutritional problems occur frequently, many can be managed by more careful supervision.

Approximately one-fourth of the patients who survive total gastrectomy experience some dysphagia and difficulty in eating owing to narrowing and spasm of the esophagojejunal anastomosis. If definite obstruction is shown to be present by roentgenologic examination of the esophagus or by esophagoscopy, it can be relieved by dilatation with a bougie and this will, in most instances, correct the dysphagia (Fig. 9). Difficulty in swallowing does not always indicate recurrent carcinoma at the site of the anastomosis and the presence or absence of recurrent carcinoma can always be established by esophagoscopy; biopsy can be done if indicated.

Anemia is not uncommon after total gastrectomy but varies considerably from patient to patient. Practically all of our patients who survived operation, eventually required treatment for anemia. The commonest anemia seen after operation is that of a hypochromic state owing to iron deficiency. This is easily treated with doses of ferrous sulfate. In a few patients a macrocytic, megaloblastic type of

Fig. 10. Recurrent carcinoma in esophagus 6 months after operation. Total gastrectomy was performed for mucinous carcinoma of the fundus with involvement of the lower end of the esophagus.

anemia will develop but usually at a much later period. However, appropriate blood studies should be carried out at regular intervals so that the development of anemia may be recognized early and proper treatment instituted when it is found.

ReMine and Priestley stated that a satisfactory concentration of hemoglobin was not maintained without the use of iron or other medication in any of their 13 patients who survived 5 years or more, but none developed an addisonian type of anemia.

MacDonald, Ingelfinger, and Belding (22) stated that an anemia similar to pernicious anemia will develop after total gastrectomy if the patient survives long enough, and such has been our experience. This type of anemia, however, responds readily to appropriate therapy.

When diet and nutrition were carefully supervised most of our surviving patients developed a good appetite and were able to carry on their usual activity, but became fatigued much more readily. Loss of weight, failing appetite, and inability to eat were in most instances evidences of recurrent carcinoma (Fig. 10). Sweet has pointed out that in his series of cases when carcinoma did not recur, the patients led active and useful lives. This has also been our experience but it is apparent that their activity is often below par and they have a tendency to greater weariness. We believe that, following total gastrectomy, patients are able in most instances to maintain a reasonable state of health, to ingest a sufficiently high caloric diet if nutritional instruction has been adequate, and to live a reasonably happy and comfortable life. It must be conceded, however, that the problems of nutrition, anemia, digestion, and weight maintenance are vastly more complicated than when partial gastrectomy is done.

CONCLUSIONS

A series of 202 cases of total gastrectomy is reported, of which 184 were malignant tumors. As would be expected, the mortality rate in the earlier group of cases from 1927 to 1943 was prohibitively high (34.6 per cent). With experience in operative technique and improvements in preoperative preparation and postoperative care, the mortality rate in the later group of 127 cases was decreased to 8.7 per cent.

From data at hand, it can be concluded that total gastrectomy does not increase the 5 year survival rate. A high curability rate will result only when patients with gastric cancer are operated on earlier and at a time when the malignant tumor is still limited to the stomach and has not invaded the surrounding lymphatic and vascular drainage areas.

Of those patients who survived total gastrectomy, 26.2 per cent lived 3 years or longer and 14.1 per cent lived 5 years or longer.

The employment of total gastrectomy as a routine method of treatment in cases of cancer of the stomach is not advocated nor have sufficient data been collected to justify the use of such a radical procedure. In selected cases, however, total gastrectomy deserves a thorough trial.

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Fig. 10. Recurrent carcinoma in esophagus 6 months after operation. Total gastrectomy was performed for mucinous carcinoma of the fundus with involvement of the lower end of the esophagus.

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A COMPARATIVE STUDY OF THE VENOUS VALVES IN THE LIMBS

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WHEN a subject becomes of pathologic and clinical interest there is usually a desire for further anatomic and physiologic knowledge of the organs concerned. Varicose veins, though recognized for a long time, now have much more thought devoted to them than ever before. On the other hand the sequelae of thrombosis of the deep veins of the leg have been practically ignored by clinicians until the last few years but are now attracting much attention. These conditions are virtually confined to the human race, lower animals being more or less immune. As varicose veins are generally regarded as a penalty of the erect posture some illumination may be shed upon the problem by a study of the incidence of venous valves in the limbs of certain animals. It was decided to select rhesus macaque monkeys, dogs, and cats for comparative studies because they are fairly equal in size and readily available. No examination of human veins has been made as the information on this point is already available from the articles by Basmajian, Kampmeier and Birch, and Kosinski, and the differences in size between the animals mentioned and man might well invalidate any deductions made from such a comparison. The macaque monkey often walks on two legs and so it might be expected that the venous return from its hind limbs would face much the same difficulties as in man.

METHODS

All the limbs of 8 animals of each series were examined. Findings are therefore available from 16 hind limbs and 16 fore limbs of monkeys, dogs, and cats.

The veins to be examined were dissected out and removed. They were then slit up their whole length and the number and position of valves noted. The smaller veins were opened under water and examined with a magnifying glass.

The following veins were examined:

Hind limb—(a) the femoral and popliteal veins down to the formation of the popliteal by the anterior and posterior tibial veins (These latter, both comprising a pair of venae comites, were too small to be split open in their entirety, and so they were not examined); (b) the long saphenous vein from its upper end to the ankle; (c) the short saphenous vein from its upper end to the ankle.

Fore limb—(a) the axillary and brachial veins from the clavicle to approximately the level of the elbow joint; (b) the cephalic vein from its upper end to the wrist.

The long saphenous vein in the monkey and the short saphenous and cephalic veins in the cat were very narrow and, therefore, difficult to open. As a result, in some specimens only a part of these veins could be examined.

It was considered that, as the number of valves might be related to the amount of muscle present, an attempt should be made to compare the musculature in different limbs. As it forms the bulk of the tissue in these limbs it was decided that the limb circumference would give a reasonably accurate method of comparing the amount of muscle present in different species and in different limbs of the same species. The circumference of both major segments of each limb was therefore measured by a string stretched firmly round it. In the leg the string was applied midway between knee and ankle and in the forearm midway between elbow and wrist. In the thigh and arm it was applied just below the point where the limb began to broaden out at its attachment to the trunk. The average circumferences are given in Table I.

The following method was used to compare the distribution of valves. The lengths of each vein in each species were added together and

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then divided by the total number of valves in these veins. For example, the total length of the femoral veins examined in the 16 monkey lower limbs was 187 centimeters; the number of valves found in them was 16, thus giving a distribution of one valve to approximately every 12 centimeters. In this way the frequency of valves in different veins and species could be compared with greater ease and accuracy than by comparing single animals (Table II).

In specimens in which they were available the inferior vena cava, and the common and external iliac veins were also examined for valves.

FINDINGS

Hind limbs. It was found that valves, in the veins examined, were most frequent in the dog, with the monkey and cat veins about equally supplied. In each species valves were commoner in the superficial than in the deeper veins.

Table II shows that in the femoral vein valves were most frequent in the dog and least so in the monkey, the only one of the animals which normally adopts an upright posture. In each animal one of the saphenous veins was much wider than the other. In the dog and monkey the short saphenous was wider than the long saphenous and had much more frequently spaced valves. In the cat the wide long saphenous vein had approximately twice as many valves as the narrow short saphenous vein. Thus the greater the diameter of the superficial vein the more valves it seems to possess. Although in each species the femoral vein had a cross section about twice as great as that of the wider of the saphenous veins it did not have more valves, and in the dog and monkey it possessed only about half as many.

Although the difference was not marked, valves tended to be commoner in the thigh than the leg. This, of course, only applied to the superficial veins as the deep veins of the leg were not examined. It was most noticeable in the dog, which had the most muscular limb. The limb circumference in dogs was substantially greater than those in monkeys, which in turn were greater than those in cats (Table I).

Fore limbs. The findings were closely parallel to those in the hind limbs. The dog, which had the greatest limb circumference, had easily the most frequently spaced valves in superficial and deep veins. The cat was rather better supplied, with valves in both veins, than the monkey, though the former had a smaller limb circumference. In the dog and monkey, valves were commoner in the superficial than deep veins and were approximately equal in both sets in the cat.

TABLE I. — AVERAGE LIMB CIRCUMFERENCES IN THE MONKEY, DOG, AND CAT

	Monkey	Dog	Cat
Thigh, cm.	17	22	14
Leg, cm.	11	15	8.5
Arm, cm.	12.5	15.5	10
Forearm, cm.	10	11.5	7.5

DISCUSSION

From these findings the following broad conclusions emerge:

1. The dog is the most muscular of the three types examined and its veins are supplied most freely with valves.

2. The superficial and deep veins of macaque monkeys and cats are almost equally supplied with valves in both limbs, although the monkey is rather more muscular.

3. In the dog and cat, the distribution of valves is almost identical in fore and hind limbs in both sets of vessels. In the monkey the frequency is practically the same in the short saphenous and cephalic veins. (Owing to the narrowness of the long saphenous vein the results in this vessel are not considered to be sufficiently accurate to be used in arriving at any conclusion.) The femoral and axillary veins of the monkey have few valves with the latter having slightly the greater number.

TABLE II. — AVERAGE DISTANCE BETWEEN VALVES IN VARIOUS VEINS

	Monkey	Dog	Cat
Hind limb Femoralpoplitealvein, cm.	12	3.5	5
Long saphenous vein, cm.	—	3.1	5
Short saphenous vein, cm.	6	2	11.5
Fore limb Axillary brachial vein, cm.	7.5	3.6	5.3
Cephalic vein, cm.	6.3	2.2	4.9

Whether this is of any significance is doubtful as there are so few valves in either vessel.

4. Valves are commoner in the superficial than in the deep veins.

If valves are intimately related to posture they should be more common in the hind limb of the monkey. It was found, however, that valves were much less common in the hind limb of the monkey than in the dog, and slightly less so even than in the cat which had a smaller limb. In all three species valves were about equally distributed in fore and hind limbs. This is a reasonable expectation in the dog and cat, but if they are an antigravity mechanism they might be expected to be more numerous in the hind limb of the monkey than in the fore limb. It, therefore, seems that the coincidence of valves is not closely related to the posture of the animal and supports the view expressed by Franklin in 1937 and Kampmeier and Birch in 1927 that the main function of valves is not to counter the effects of gravity. It should be noted that in these animals the presence of valves between the termination of the common iliac vein to the point where the long saphenous vein joins the femoral vein is similar to that in man. Basmajian found a valve in this segment in about two-thirds of cases, and an approximately similar distribution was found in this series. The presence of a valve in these veins is of significance in interrupting the column of blood stretching from the right auricle to the hind limb.

Franklin's theory of the functions of valves is that they protect capillaries and venules from sudden excessive rises of blood pressure during muscular exercise. This view could be supported by the findings mentioned. That the incidence of valves is related to the amount of muscle is suggested by the following facts: (1) The dog's limbs are considerably more muscular than those of the other two animals and its veins are much better supplied with valves. (2) In the same species the biggest and most muscular animals are best supplied with valves. This was a particularly noticeable feature in the dog. (3) Valves tend to be more frequent in the proximal than the distal segments of the limbs, a finding which can be related to the greater size of thigh and arm. As already stated, this observation refers to the superficial veins only.

One finding, however, conflicted with the facts presented; the monkey, though more muscular than the cat, had slightly fewer valves, but this alone does not necessarily invalidate the other arguments that valves are safeguards to small veins and capillaries during muscle contractions.

CONCLUSION

From the evidence presented it does not appear that the adoption of a partially erect posture leads to an increase in the number of venous valves in the hind limb. The valves indeed do not seem to be concerned particularly with countering the effects of gravity. Since the erect posture is bound to increase venous pressure in the hind limb this apparent lack of any compensatory mechanism is likely to lead to an increase in disorders of the veins of the human lower limbs.

The conclusion reached was that the function of valves is to counter the effects of muscular action and prevent a rapid rise in pressure in capillaries and venules during muscle contractions.

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ABNORMAL PLASMA PROTEOLYTIC ACTIVITY

Diagnosis and Treatment

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IN 1893 the French biochemist Dastre published his observations made during the process of perfecting a procedure for the quantitative chemical determination of fibrin. As a source of fibrin this investigator used fresh blood drawn from living dogs and in the course of repeated determinations found that the fibrin yield was reduced as the rate and magnitude of phlebotomy was increased. Subsequently Dastre proved this chemical procedure to be accurate and postulated that the decreased yield was due to actual destruction or lysis of fibrin and, therefore, designated this phenomenon fibrinolysis. In 1937 the effect of fibrinolysis on blood clotting became widely publicized when Yudin demonstrated the possibility of employing cadaver blood, without anticoagulants, for transfusion purposes. Following phlebotomy the blood clotted but subsequently reliquefied and remained in a fluid state thereafter. For such phlebotomies Yudin wisely chose bodies that were subjected to shock prior to death.

Subsequently many investigators partially clarified the problem of fibrinolysis and plasma proteolytic enzymes as described in the extensive and excellent review of MacFarlane and Biggs (14). Currently the concept of plasma proteolytic enzymes embodies a balanced enzyme system in human plasma which consists of the active enzyme, its precursor, and its inhibitor. The active enzyme has been designated plasmin and its inactive or precursor form has been termed plasminogen. As a countercheck of plasmin there is postulated an antienzyme or enzyme inhibitor which is designated antiplasmin. Such standard terminology is highly recommended and will be used throughout this communication. For editorial simplicity the term plasminemia is used in this report to denote the condition in which there is an increased quantity of circulating plasmin.

Plasminogen and plasmin have been shown to reside in the globulin fraction of the plasma proteins whereas antiplasmin is associated with the albumin fraction. The majority of investigations indicate that plasmin is not fastidious in its proteolytic activity but rather is capable of digesting fibrinogen, prothrombin, plasma and serum prothrombin accessory substances, casein, gelatin, and other proteins as well as fibrin. Although recent reports are conflicting as to the speed of digestion of fibrin and fibrinogen by the plasma proteolytic enzymes these seemingly divergent results have been reconciled by standardization of technique. Significant differences in the fibrinolytic as opposed to the proteolytic activity of serum have also been demonstrated. These differences appear clear-cut, and the basic working concept of plasmin being primarily proteolytic rather than solely fibrinolytic is recommended.

It is immediately apparent that such an enzyme circulating freely in the blood stream of man is capable of effecting serious alteration in the coagulation mechanism and thereby causing fatal hemorrhage in certain instances. Under such circumstances ensuing shock may then alter the vascular factors of hemostasis through endothelial hypoxia causing widespread vascular damage. This in turn may result in further loss of blood and plasma from the circulation and thereby augment the shock. A vicious cycle becomes established and must be interrupted or death from hemor-

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rhage and shock may ensue. The resultant clinical picture has been termed "fibrinolytic purpura" by Stefanini. In view of the possibility of this plasma enzyme system losing its equilibrium and becoming overwhelmingly proteolytic, it becomes important to recognize abnormal plasmin activity as one of the many factors influencing the effectiveness of the hemostatic mechanism.

Since it is believed that plasma proteolytic phenomena are much more frequent than has heretofore been considered, it is believed worthwhile to report some of our experiences in the study and management of a number of patients with plasminemia.

METHODS

Coagulation time of venous blood. A modified Lee-White method as previously described by Patek and Stetson was employed. The normal range for this method is 6 to 12 minutes.

Bleeding time. The method of Duke was employed, the normal range being 2 to 4½ minutes.

Plasma prothrombin concentration. The method of Quick was used.

Plasma fibrinogen concentration. The sodium sulfite method described by Campbell and Hanna was used, the normal range being 200 to 400 milligrams per cent.

Assay of serum proteolytic activity. The method of Downie and Cliffton, modified in part, was employed. The albumin fraction of the serum protein, and thus, theoretically, serum antiplasmin, is removed by iso-electric precipitation. This leaves the plasminogen or plasmin of the globulin fraction unopposed in their activity in the final reaction mixture. This method measures serum proteolytic activity as a function of tyrosine released from casein over a given period of time (24 hours). It has been shown that there is a straight line relationship between the negative logarithm of transmittance (optical density) and milligrams of tyrosine measured. Therefore, the negative logarithm of transmittance was used as the index of proteolytic activity. It may be shown[1] that any transmittance below .41 (−log.41 = .393) is statistically significant as an indication of abnormal proteolytic activity.

[1]For normal controls N = 10; X = .213; standard deviation = .043 and standard deviation of the mean = .017.

CASE REPORTS

CASE 1. C.McM., a 62 year old colored male, was admitted to the hospital because of urinary obstruction due to benign prostatic hypertrophy. Preoperative studies, including a bleeding and coagulation time, were normal. Under spinal anesthesia a transurethral resection of the prostate gland was performed. The gland was considerably larger than anticipated and 117 grams of prostatic tissue were removed, the operation lasting 1 hour and 40 minutes. During the procedure there was a moderate fall in blood pressure which was corrected by the intravenous administration of 1,000 milliliters of whole blood. Immediately following operation the patient started to bleed profusely through the urethral catheter and within 30 minutes the systolic blood pressure had fallen to 80 millimeters of mercury. A specimen of blood drawn at this time from the femoral artery for plasmin determination clotted within a normal range of time. Routine shock measures, including blood transfusions, were instituted and the blood pressure gradually rose to a normal level and became stabilized. Four hours after operation there was definitely less bleeding and improvement continued thereafter. Throughout the 6 hours following operation the patient received a total of 2,500 milliliters of whole blood intravenously, but at no time did he receive serum albumin. Eighteen hours after operation there was minimal bleeding through the urethral catheter. On the first postoperative day blood studies showed no abnormality except for the anticipated moderately elevated leucocyte count. Plasma prothrombin activity was 100 per cent of normal, and the coagulation and bleeding times were within normal limits. The specimen of arterial blood, drawn aseptically after operation on the previous day, was found to have completely liquefied 18 hours later. Convalescence was complicated by a transient period of oliguria followed by diuresis and recovery. No laboratory evidence of a hemolytic transfusion reaction was found. Pathologically the prostatic tissue was characteristic of benign prostatic hypertrophy.

It is believed that this patient developed plasminemia during operation, since bleeding from the prostatic bed had increased considerably by the time the operation was completed. It is presumed that gradual diminution of abnormal bleeding was effected through multiple blood transfusions, the transfused blood containing sufficient protein substrate as well as antiproteolytic factors to partially neutralize the circulating proteolytic enzyme. The serum from blood drawn postoperatively, but

prior to treatment, was found to have abnormally high proteolytic activity as shown in Figure 1. Posttreatment serum was not available for assay.

CASE 2. J.V., a 67 year old white male, was admitted to the hospital for prostatectomy to correct obstructive urinary symptoms caused by benign prostatic hypertrophy. He had previously undergone an abdominoperineal resection of the rectum for adenocarcinoma, this being complicated by a severe hemolytic transfusion reaction from which the patient recovered satisfactorily. Preoperative studies on this admission revealed evidence of moderate liver damage. A transurethral prostatic resection was done under spinal anesthesia supplemented with sodium pentothal, and 38 grams of prostatic tissue were removed without difficulty. During the procedure, which lasted approximately 1 hour and 20 minutes, only moderate bleeding was encountered and the blood pressure remained stable.

Shortly after operation bleeding through the catheter became progressively more severe, and the patient's blood pressure fell to shock level. Intravenous glucose followed by whole blood was given, and 3 hours postoperatively it was necessary to institute intra-arterial blood transfusions because bleeding had become more profuse and the blood pressure unobtainable. Thereafter, the arterial pressure gradually returned to normal, but 4 hours postoperatively oozing of blood from all venipuncture sites was noted. A blood sample for study was withdrawn from the patient at this time. Separately, 100 milligrams of toluidine blue and 100 milliliters of a 25 per cent solution of low salt human serum albumin were empirically administered intravenously to combat possible hyperheparinemia or plasminemia, respectively, this being done because a differential diagnosis between these two states was impossible prior to observation of the blood clot in vitro. The unaltered blood sample failed to clot over an observation period of ½ hour, and, furthermore, the addition of a large amount of powdered bovine thrombin to the blood sample failed to effect clotting, thereby indicating afibrinogenemia rather than hyperheparinemia. Similarly, the prothrombin time by the one stage method was infinitely prolonged. In view of these findings it was concluded that plasminemia was responsible for the unusual bleeding. Subsequently, this patient's plasma lysed a normal homologous blood clot lending further support to the diagnosis of plasminemia. Therapy thereafter consisted of whole blood transfusions and the intravenous administration of 100 milliliters of serum albumin every hour for the subsequent 4 hours. At the end of this regime, that is approximately 9 hours postoperatively, the blood pressure was 180/90, but bleeding continued. Subsequently, the blood pressure progressively declined and the patient expired 12 hours after operation, having received a total of 4,000 milliliters of whole blood and

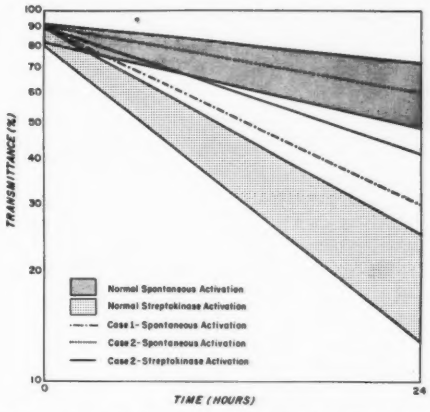


Fig. 1. Quantitative serum proteolytic activity in the sera of 10 normal individuals and Cases 1 and 2.

500 milliliters of serum albumin. Necropsy revealed multiple hemorrhages throughout all viscera.

The blood of this patient demonstrated complete failure of the clotting mechanism. There was a total absence of figrinogen as evidenced by failure of clotting on the addition of potent bovine thrombin and the prothrombin time was infinitely prolonged. It should be mentioned that the one stage prothrombin technique under these circumstances is not a valid assay for prothrombin since fibrinogen is one of the prerequisites for the end point of the test. The absence of fibrinogen was considered the result of abnormal proteolytic activity since the pretreatment blood sample proved capable of lysing a normal homologous blood clot. Whole blood was administered to combat shock and provide substrate for the enzymes, and serum albumin was employed to provide additional antiproteolytic factors to directly combat plasminemia. Unfortunately, the pretreatment blood specimen was discarded, but serum obtained from the patient after therapy had been given was available for study. This serum exhibited spontaneous proteolytic activity within the normal range, but decreased activation with streptokinase as shown in Figure 1. These findings are considered the result of excess antienzyme which may have been "bound" to the plasminogen or plasmin consequent to the content of antiplasmin in the whole blood and

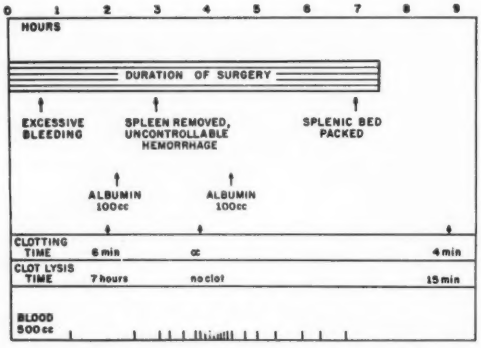


Fig. 2. Graphic representation of Case 3 showing the relationship of duration of surgery, blood coagulation and lysis times, blood transfusion, and serum albumin administration.

serum albumin used in treatment. Consideration of these alternatives will be taken up later. It is believed that progressive and continued bleeding in this instance was largely on the basis of vascular hypoxia with resultant increased capillary permeability.

CASE 3. L.C., a 67 year old colored male with idiopathic hypersplenism, was admitted to the hospital for splenectomy. Physical examination revealed slight pallor and splenomegaly, and peripheral blood studies revealed a persistent pancytopenia. Bone marrow obtained by needle aspiration from a vertebral spinous process and the sternum was hyperplastic; erythrocyte osmotic fragility was normal; function tests of the liver and adrenal cortex were normal; and prothrombin activity was 100 per cent of normal.

Splenectomy was undertaken under combined ethylene and ether anesthesia. From the very beginning of the procedure there was inordinate blood loss, and great difficulty was encountered in effecting hemostasis in the incision. Two hours after initiation of the operation a control coagulation time of the patient's blood was 6 minutes, and there was good clot retraction (Fig. 2). Since a normal clotting time militated against a circulating anticoagulant, a tentative diagnosis of plasminemia was made and 100 milliliters of serum albumin were administered intravenously. Three hours after starting the operation the spleen was removed with coincident massive hemorrhage. Venous blood drawn at this time was incoagulable. Since clotting failed to occur when powdered human thrombin and pressure were applied to the bleeding area in the abdomen, fibrinogen was presumed to be low or absent. An additional 100 milliliters of serum albumin were given intravenously and large quantities of blood were used in an effort to combat shock as well as to replace deficient coagulation factors and erythrocytes. Pressure, packs, cautery, and gelfoam had little effect in stemming the resistant hemorrhage. The splenic bed was finally packed with 10 large vaginal packs which were allowed to protrude to the outside and the incision was left open. The patient was returned to the ward in a remarkably fair condition with the systolic blood pressure at its preoperative level of 160 millimeters of mercury. During the 7½ hour operation he had received a total of 21 units (10,550 ml.) of whole blood and 200 milliliters of serum albumin. The control clot, which had been obtained 2 hours after initiation of the operation and which had been maintained at 37 degrees C., was seen to have completely disintegrated 7 hours after venipuncture, thus confirming the initial impression of plasminemia. Venous blood drawn 1 hour after termination of the operation showed a coagulation time of 4 minutes, with complete dissolution of the clot in 15 minutes under standard conditions (Fig. 2). Unfortunately these sera were not available for quantitative proteolytic assay.

The patient had no further hemorrhagic episodes nor did he receive additional therapy in the form of whole blood or serum albumin. Subsequently his wound was closed secondarily, convalescence was uneventful, and the pancytopenia disappeared. Studies 4 months later showed the patient to be in good health, having had no interim episodes of bleeding.

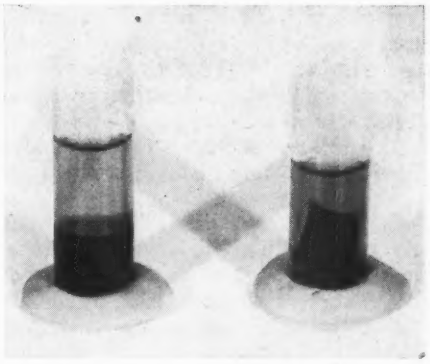
Plasminemia was demonstrated in this case and what appeared to be imminent fatal hemorrhage is believed to have been corrected by the combined therapeutic measures employed. This case exemplifies the rationale of supplying coagulation factors as substrate in the form of whole blood or plasma while endeavoring to equilibrate the plasma proteolytic enzyme system by the use of serum albumin for its antienzyme content.

CASE 4. M.S., a 26 year old colored female, who 14 months previously had been delivered of twins uneventfully, was admitted to the obstetric service at term and in early labor. Eight hours after admission she delivered a normal child with minimal blood loss. Manual removal of an adherent placenta was necessary, and careful examination revealed no tears in the cervix or uterus. Thirty minutes after this procedure there was excessive bleeding associated with evidence of uterine relaxation. Treatment with pitocin and ergotrate was effective in contracting the uterus but 4 hours later there was excessive vaginal bleeding accompanied by a weak and rapid pulse. Routine shock measures, including whole blood transfusions, were instituted; and the uterine cavity was again examined and, on this occasion, packed. During this procedure the patient aspirated a large quantity of vomitus resulting in transient apnea. Following restoration of an adequate airway, bleed-

ing was also observed from the nose, mouth, and venipuncture sites, as well as from the uterus. At this point spontaneous lysis of her blood clot was demonstrated 15 minutes after normal coagulation had occurred (tube a, Fig. 3). Other studies at this time revealed a normal platelet count, a plasma prothrombin concentration of 32 per cent of normal and a plasma fibrinogen of 456 milligrams per cent. Plasminemia was considered to be present and treatment with serum albumin was instituted. Within 1 hour the integrity of the clot improved considerably and showed only minimal lysis which required 24 hours' observation for demonstration (tube b, Fig. 3). During 18 hours the patient received a total of 4,000 milliliters of whole blood and 800 milliliters of serum albumin. The blood pressure became stabilized at an average level of 140/90 and bleeding ceased. The patient, however, became increasingly dyspneic and developed signs of pneumonia, considered to be on the basis of aspiration. No further bleeding was encountered and in spite of all efforts in treating the chemical pneumonia the patient expired 60 hours postpartum.

This case presented the problem of plasminemia developing during shock associated with postpartum hemorrhage and adherent placenta. At no time was there demonstrated incoagulability of her blood to suggest entry of amniotic fluid into the circulation with resulting intravascular clotting through the thromboplastic effect of this fluid. In addition, the normal plasma fibrinogen content militated against amniotic fluid embolism. With prompt recognition of plasminemia and immediate institution of therapy it was possible, within the short time of 1 hour, essentially to obliterate proteolytic activity and control the bleeding.

CASE 5. R.V., a 36 year old colored female, was admitted to the hospital 1 hour after receiving multiple gunshot wounds involving the head, chest, abdomen, and arms. On arrival she was alert and the blood pressure was 110/95. Because of obvious intraperitoneal injury a laparotomy was performed after emergency treatment of the other wounds. The right colon had been penetrated, there were 4 perforating wounds of the jejunum, and a large retroperitoneal hematoma was present. The body and part of the tail and head of the pancreas were injured by the passage of a bullet which had also severed the common bile duct. The colon and jejunum were repaired, and a modified Whipple operation was performed. Blood pressure was maintained at satisfactory levels with the aid of multiple transfusions of whole blood until the fifth hour of the operation when generalized oozing of blood from the entire operative field as well as venipuncture sites was noticed. Blood obtained at this time had a



a b

Fig. 3. Case 4. Unaltered venous blood showing complete dissolution of the blood clot in the tube on the left (tube a) after 15 minutes' observation. The tube on the right (tube b) shows only minimal lysis of the clot after 24 hours' observation, this blood having been drawn posttherapeutically 1 hour after that in tube a.

normal platelet count and a clotting time of 6 minutes. Within 1 hour this clot completely liquefied, and a tentative diagnosis of plasminemia was made. Promptly after the onset of shock and generalized bleeding, 100 milliliters of serum albumin were given intravenously, and within 30 minutes the surgeons noticed improved hemostasis, and the blood pressure had risen to 90/50. The hemorrhagic tendency appeared to be temporarily corrected and the operation was completed. During the 9 hour operation the patient received a total of 24 units (12,000 ml.) of whole blood and 3 units (300 ml.) of serum albumin. In order to secure an adequate airway a tracheotomy was done following surgery. In the subsequent 24 hour period the patient received another 4 units of serum albumin but no further transfusions of whole blood. Generalized bleeding was not encountered thereafter. The patient was doing moderately well until the tenth postoperative day when, as a result of massive hemorrhage from erosion of the right common carotid artery by the tracheotomy tube, she quickly expired.

This case represents "fibrinolytic purpura" which was corrected by vigorous therapy. Since the hemorrhagic tendency was noted clinically at about the same time shock began it is difficult to assess the role of shock in its etiology. In addition it could be speculated that liberation of tissue enzymes, such as trypsin from the severely traumatized pancreas, contributed to the chain of proteolytic events observed in this instance. One would not, however, anticipate that the antiplasmin of human serum albumin would neutralize the

proteolytic activity of trypsin since antiplasmin is considered a specific antienzyme for plasmin and not for trypsin. The cessation of bleeding, following treatment with serum albumin and whole blood, suggested that plasminemia was probably the cause of this patient's unusual bleeding.

RESULTS

Figure 1 depicts graphically quantitative serum proteolytic activity of Cases 1 and 2, as well as that of 10 normal subjects, the latter being assayed for both spontaneous and streptokinase activated proteolytic activity. Spontaneous proteolytic activity of normal serum is apparent by this method, the range after 24 hours incubation being 75 to 50 per cent transmittance. These normal results are in contrast to the marked spontaneous serum proteolytic activity of Case 1. The serum in this instance was collected prior to therapy at a time when the patient was bleeding freely and the clinical impression of plasminemia was entertained. One, therefore, would anticipate increased spontaneous proteolytic activity in this pretreatment serum on the basis of excess active enzyme and such was the case. The serum of Case 2 which was obtained after treatment with serum albumin and whole blood showed spontaneous activity within the normal range.

Proteolytic activity of normal serum by streptokinase activation was marked with a range of 26 to 13 per cent transmittance. These results constitute strong evidence that plasmin is normally present in plasma in an inactive precursor state. Serum of Case 1 was not subjected to streptokinase activation since a positive result was already evident in the form of increased spontaneous proteolytic activity. The posttreatment serum of Case 2, however, demonstrated definite resistance to such activation. As an explanation of this finding one might consider that there existed a relative unavailability of plasminogen in this serum as compared to normal serum. The mechanism of this supposed hypoplasminogenemia, however, is not so simple. In general the demonstration of the total quantity of active enyzme in vitro is dependent upon: (1) the amount of enzyme precursor available and (2) the presence of antagonists to either the enzyme precursor or the active enzyme itself. It is not possible by the technique employed in these experiments to determine unequivocally which one of these factors is responsible for the observed results.

DISCUSSION

The 5 cases included in this report presented the startling clinical picture of overwhelming hemorrhage, and indeed, 1 of the patients expired rapidly from exsanguination. It is imperative to point out, however, that plasminemia may be present with little or no clinical manifestations, such activity at times being demonstrable only by careful and detailed laboratory studies. In order to develop an understanding of this condition for diagnosis and treatment, it becomes necessary to review some of the pertinent observations that have been made previously.

Clinical investigation has indicated that shock may precipitate the conversion of plasminogen to plasmin in many instances. The reports of plasminemia in humans with severe burns, in peptone shock in dogs, in shock due to typhoid vaccine injection in man, the plasma transfusion reaction, and the reports of many others suggested this common denominator. Lewis and Ferguson have intimated from their studies, however, that the activation of plasminogen in and of itself causes hypotension which in turn can be corrected by the administration of soybean trypsin inhibitor. Thus it has been suggested that shock may be the result rather than the cause of plasminemia. MacFarlane and Biggs (13) and Biggs, MacFarlane, and Pilling (2) on the other hand have demonstrated plasmin activity in man following such seemingly divergent stimuli as fear, exercise, trauma, and parenteral administration of adrenalin. The studies of these authors clearly show that some 50 per cent of their preoperative patients, *who were not in shock*, exhibited plasminemia without hemorrhagic phenomena. Similarly, it is also significant that plasminemia was demonstrated in approximately 50 per cent of their postoperative patients even though the operations varied from such simple procedures as incision and drainage of a furuncle to such

major undertakings as bowel resection. Cliffton has in the main confirmed the results of these authors.

Because of these findings MacFarlane postulated the alarm reaction of Selye as the basis of activation of plasminogen, whether or not shock supervened, since stress was considered to be the outstanding constant in the patients he studied. Exploring this idea, Biggs, MacFarlane, and Pilling were able to demonstrate spontaneous plasminemia in normal healthy adult males following the subcutaneous injection of 2 milliliters of a 1:1000 solution of adrenalin. Adrenalin was incapable of causing this reaction in vitro. To complement these observations Cliffton has shown that steroid induced plasminemia in man is in reality due to activation of plasminogen to plasmin rather than associated reduction in antiplasmin activity. This latter observation is at variance with the usual finding in which human subjects develop decreased antiplasmin titers in association with fear, x-ray treatment, and trauma. In view of these and other similar studies, the general alarm reaction has been seriously considered to be the basic mechanism for abnormal plasma proteolytic activity. The sequence of events is not quite so simple as this, however, since spontaneous plasmin activity has been demonstrated in patients with Addison's disease following the subcutaneous injection of adrenalin. At necropsy the adrenal cortices of these patients were found to be completely destroyed. In addition, the observations of Cliffton cited previously also suggest other mechanisms.

Recent observations in cases of afibrinogenemia due to amniotic fluid infusion or "emboli" have revealed associated abnormal plasma proteolytic activity. Reid and associates have suggested that this may represent the body's reaction to excessive fibrin deposition consequent to the thromboplastic activity of amniotic fluid. This did not appear to be the mechanism of bleeding in Case 4 of this report, however, since the fibrinogen level was normal.

The exact mechanism of activation of the plasma proteolytic enzymes, therefore, is still open to speculation. There is considerable evidence at the present time, which indicates that such activation probably originates in the tissue cells and that shock may, in an as yet unknown fashion, liberate these activators. For example, the fact that Tagnon and Petermann (21) have been able to demonstrate abnormal proteolytic activity in the blood of the pulmonary vein prior to its appearance in the pulmonary artery suggests the presence of a potent activator in lung tissue. This hypothesis was strengthened by these authors who have demonstrated an activator of plasminogen in many tissues, and particularly in lung tissue. Mathey and associates have further confirmed these observations and are of the opinion that the activator of plasminogen originates within the lung, and, therefore, they caution that thoracic surgery is particularly prone to result in plasminemia with all of its possible dire sequelae. Astrup and Permin have also shown that animal tissue cells contain a substance which activates plasminogen, and suggest that such activation is a general property of all tissue cells. In this respect, cancer itself may be related since Coon and Hodgson report a patient with bronchogenic carcinoma who had persistent plasminemia and fibrinogenopenia. Following surgical removal of the tumor, plasminemia disappeared and the plasma fibrinogen level rose to 4 times the preoperative concentration. This particular tumor, however, may represent a special instance since it originated in tissue now shown to possess great plasminogen activator ability. Mention should be made, however, that plasminemia is not the usual finding in neoplastic states as pointed out by Cliffton who, on the contrary, found a high antiplasmin titer and an associated low plasmin titer in patients afflicted with cancer.

A variety of pathologic states have been shown to have an associated plasminemia. Significantly, Ratnoff has demonstrated abnormal proteolytic activity in the plasma of patients with hepatic cirrhosis as well as in patients with obstructive jaundice. In this situation plasminemia, coupled with existing faulty elaboration of fibrinogen and prothrombin by the damaged liver, may well explain the hemorrhagic diathesis so often observed when a surgical procedure is carried out on such patients. This may well have been a con-

tributing factor in Case 2 who had preoperative laboratory evidence of liver damage. Instances of marked proteolytic activity have also been reported in association with pancreatic surgery. Such observations have been considered confirmatory evidence that plasmin is, in effect, trypsin. There is little question that both plasmin and trypsin are proteolytic enzymes and are probably capable of producing a very similar, if not identical, clinical picture in man once either becomes freely circulating in the blood. It does not follow, however, that they are one and the same enzyme. The excellently planned and executed work of Kaplan clearly distinguishes plasmin from trypsin and there seems little value in belaboring this point.

The finding of plasminemia immediately following transurethral prostatic operation in 2 (Cases 1 and 2) of the patients herein reported is particularly interesting in view of the fact that human semen has been found to have a high concentration of a proteolytic enzyme which originates in the prostate gland. This enzyme, responsible for the liquefaction of semen, is considered by Huggins and Neal to be similar to the proteolytic enzyme associated with hemolytic streptococci. No conclusion, however, can be drawn as to its identity with plasmin. In addition to these observations, Tagnon and associates (22) have reported cases of extensive metastatic prostatic carcinoma associated with marked plasma proteolytic activity. These latter authors point out the analogy of increased plasma proteolytic activity in these patients to other cases of metastatic carcinoma of the prostate with an elevated serum acid phosphatase. It is not unreasonable to suppose that the prostatic proteolytic enzyme and prostatic acid phosphatase are produced by the same cell. Since trauma to the prostate gland by massage alone has been reported to cause a transient elevation of serum acid phosphatase it is quite feasible that the more severe trauma of a prostatic operation could result in the intravascular release of all other enzymes or enzyme activators produced by these cells. A situation may thus exist whereby the prostatic (semenolytic) enzyme may gain access to the blood stream in large quantities thereby overcoming the normal inhibitory action of antiplasmin or, indeed, be completely unopposed because of lack of a specific antienzyme in the plasma. Coagulation defects may thus occur and abnormal bleeding result with production of "fibrinolytic purpura" indistinguishable from that due to plasmin. Loss of integrity of the blood clot or a disturbance in the clotting mechanism obviously is a considerable hazard in transurethral prostatic surgery.

From these data it can be postulated that abnormal proteolytic activity may be encountered under the following circumstances: (1) activation of plasminogen as a result of the general alarm reaction; (2) activation of plasminogen as the result of release into the circulation of tissue activator substances (e.g., from the lung); (3) entry into the circulation of proteolytic enzymes, other than plasmin, from sources such as prostate or pancreas; (4) amniotic fluid embolism. Figure 4 depicts these concepts schematically.

In any situation, whether surgical or otherwise, in which abnormal bleeding is encountered and for which no local cause is found, one must consider the possibility of plasminemia. It should be borne in mind that a reduction in any one of the coagulation factors, such as occurs in hemophilia, plasma thromboplastin component deficiency (Christmas disease), and so forth, may alter hemostasis, but it is not within the scope of this discussion to enter into differential diagnosis of all these possibilities. Excluding these well defined conditions, most unrecognized states in the differential diagnosis of inordinate bleeding during or following operative procedures are hyperheparinemia and plasminemia. The effects of these two conditions on blood clotting are outlined as follows:

Hyperheparinemia	Plasminemia
1. Coagulation time is usually prolonged.	1. Coagulation time may be normal *or* may be infinitely prolonged.
2. Small amounts of the patient's blood will prolong the coagulation time of normal blood.	2. The patient's blood will not prolong the coagulation time of normal blood.
3. Addition of small amounts of thrombin will usually produce a clot.	3. If blood does not clot spontaneously thrombin will not cause clotting.
4. If a clot forms it does not disintegrate.	4. If a clot forms it will partially or completely disintegrate within 24 hours.

A simple screening test for confirmation of the diagnosis can be performed very easily provided such simple implements as test tubes, needles, and syringes are available. It is important to obtain blood samples from the patient as soon as abnormality of the hemostatic mechanism is suspected. Unless this is done, therapy which is given may obscure the test as it is considered to have done in Case 2. Therefore, prior to therapy, 6 milliliters of blood are withdrawn from the patient, and the two tube modified Lee-White coagulation time technique carried out aseptically. Careful observation of the blood is necessary since any one of the following processes may transpire with plasminemia: (1) the coagulation time may be normal with subsequent partial lysis of the clot; (2) the coagulation time may be normal with subsequent complete lysis of the clot; (3) there may be no coagulation. Hyperheparinemia will not cause dissolution of the blood clot and if either process 1 or 2 listed occurs, hyperheparinemia can be excluded. If the blood is incoagulable, as in the third situation, it is difficult to make an early differential diagnosis between hyperheparinemia and plasminemia. By adding thrombin to the blood in vitro these disorders can be differentiated as outlined. This simple screening test can be employed by anyone and does not require the services of a skilled technician. The primary requisite for diagnosis of plasminemia as a cause of unusual bleeding is awareness of this entity.

Once the base-line blood sample has been obtained, therapy should be instituted immediately without regard to the future integrity of the clot. This therapy consists of whole blood, low salt human serum albumin, and toluidine blue in initial doses as outlined in the following. In the event the blood sample does not clot, toluidine blue, an established antiheparin, should be given empirically because of difficulty in immediately distinguishing hyperheparinemia from plasminemia under these circumstances. This material can be injected directly from the syringe in a dosage of 5 milligrams per kilogram of body weight. Prolongation of a repeat coagulation time 30 minutes after administration of toluidine blue strongly suggests that one is not dealing with

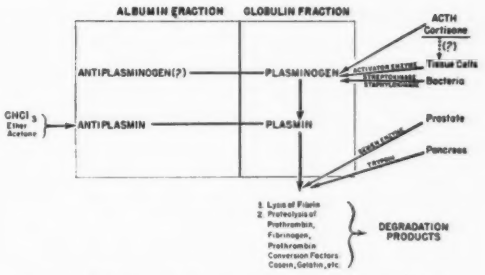


Fig. 4. Schema of plasma proteolytic enzymes and proposed mechanism of action of various compounds, bacteria, and tissue products.

hyperheparinemia. Protamine sulfate, another known antiheparin, may also be used but is undesirable as therapy for two reasons: (1) it activates the proteolytic enzyme and (2) it acts as an anticoagulant supposedly by binding thrombin. If hyperheparinemia is not present the administered protamine is in excess since there is no heparin to bind it in vivo, and it is then free to exert its antithrombic effect. Toluidine blue, fortunately, does not behave in this fashion, and thus is the agent of choice when therapy is given empirically for possible hyperheparinemia.

In the event of either an immediately normal or delayed coagulation time, therapy must also be directed toward plasminemia. This consists of the intravenous administration of: (1) whole blood and (2) low salt human serum albumin. The administration of whole blood combats abnormal plasma proteolytic activity both directly and indirectly. The *direct* attack is in the supplementation of the patient's plasma with the antiplasmin content of normal plasma. Similarly a necessary disadvantage of whole blood is its normal content of plasminogen or plasmin. This plasminogen becomes available to the patient's enzyme activating systems, and thus theoretically abnormal proteolytic activity could be enhanced. The advantages of whole blood in treatment outweigh this disadvantage, however. *Indirectly*, whole blood combats plasminemia by supplying large amounts of substrate in the form of fibrinogen, prothrombin, and other coagulation factors. By this means blood coagulation factors can be maintained above critical levels and thus partially

prevent hemorrhage. It should be recognized that the patient may be made polycythemic if transfusions are used injudiciously. Should such a situation develop, plasma alone or fraction I of Cohn (9), which contains 60 to 80 per cent fibrinogen per unit weight, may be used to supply fibrinogen substrate.

To oppose plasminemia directly low salt human serum albumin should be given intravenously. It will be recalled that antiplasmin is associated with the albumin fraction of the plasma proteins while plasminogen and plasmin are in the globulin fraction. Thus by administering albumin it is possible to supply the patient directly with concentrated antiplasmin which physiologically opposes the proteolytic action of excessive plasmin. It is recognized that intravenous low salt human serum albumin causes hemodilution through osmolarity and, therefore, will reduce somewhat the concentration of circulating fibrinogen which is of paramount importance. Serum albumin should be given in dosages of 100 milliliters every hour until there is clinical evidence of lessening of bleeding. Thereafter clinical judgment is required as to further need for this plasma derivative.

SUMMARY AND CONCLUSION

Five cases presenting the clinical picture of alarming hemorrhage due to abnormal plasma proteolytic activity are presented. Some of the possible mechanisms of activation of this enzyme and the mechanism of production of the clinical picture it may cause are discussed. Simple laboratory tests for confirmation of the diagnosis are described. A routine of therapy is presented and the rationale of such therapy is discussed.

It is concluded that plasminemia may give rise to abnormal bleeding as described. The intravenous use of low salt human serum albumin and whole blood early in this condition may be life-saving.

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SPLENECTOMY IN CHILDREN WITH IDIOPATHIC THROMBOCYTOPENIC PURPURA, HEREDITARY SPHEROCYTOSIS, AND MEDITERRANEAN ANEMIA

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EXPANDING knowledge in hematology, which has explored the varied aspects of normal and disturbed hematopoiesis has provided more precise information with regard to the pathophysiology of the spleen. While the complete functions of this organ have not been unequivocally determined, it is possible at present to set forth specific indications for its removal in certain pathologic states. In these decisions, considerable aid has been given by the broadened implications of the concept of hypersplenism. The latter provides a plausible explanation for the pathogenesis of a group of hematologic syndromes which are characterized by a reduction of one or more cellular elements in the peripheral blood with compensatory hyperplasia in the bone marrow of the corresponding cells, and the expectation that the disorder will be corrected by splenectomy. These dyscrasias have been attributed to either an overactive and unusually enlarging spleen, in which either selective storage and increased destruction of blood cells occurs, or in which the organ exerts an inhibitory influence upon a normal or hyperactive bone marrow. In either case, removal of a presumably abnormally functioning spleen has been shown to restore normal blood levels with varying degrees of success.

The purpose of this article is to review a concentrated experience of the past 5 years at The New York Hospital with several hematologic disorders of infancy and childhood, which were benefited by splenectomy. This will include 9 cases of congenital spherocytic anemia, 9 cases of Cooley's or severe Mediterranean anemia, 2 cases of the combined traits of sickle cell disease and Mediterranean anemia, and 7 cases of idiopathic thrombocytopenic purpura. While this series is acknowledgedly small, it nevertheless provides a basis for reviewing current theories in relation to the pathogenesis of each of these diseases and the provisional indications for splenectomy. It also emphasizes the need for close co-operation between the pediatrician and surgeon in the preparative and postoperative management. In this presentation, the principal criteria of each disorder will be briefly reviewed as well as the newer hematologic techniques employed not alone in establishing a diagnosis, but in providing a basis for splenectomy.

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Studies in the Department of Pediatrics were supported by grants from the Institute of Arthritis and Metabolic Diseases, United States Public Health Service (RG A-227 C4), The Children's Blood Foundation, Inc., and Mead Johnson and Company.

IDIOPATHIC THROMBOCYTOPENIC PURPURA

This entity was first described by Werlhof in 1735; the peripheral thrombocytopenia was demonstrated by Denys in 1887. The first splenectomy for the disorder was performed by Schloffer in Prague in 1916.

Recent experience has served to clarify the place of surgical therapy in the management of idiopathic thrombocytopenic purpura (ITP). Several comprehensive reports have stressed that ITP occurs in two major types, one an acute, self-limited form and the other a chronic protracted disease. Of particular importance is the fact that spontaneous remission occurs frequently in children with the majority of cases being of the acute, self-limited variety. In a recent study by Newton and Zuelzer, it was shown that of 40 children with ITP who were treated conservatively, 33 demonstrated a benign course, with spontaneous recovery occurring within 3 months in 32 of the cases. Clement and Diamond demonstrated that of a group of 93 children with

ITP, 38 made spontaneous recoveries within 6 weeks, while an additional 19 recovered within a year. In the remaining cases there was a wide range in the duration of symptoms. Hirsch and Dameshek have also stressed the distinction between the acute and chronic types of ITP and their data likewise indicate the frequency of the acute, self-limited course in the younger age groups. Rousselot found that spontaneous remissions occur rarely after the second decade. The difference in behavior of ITP in children and in adults was clearly analyzed by Newton and Zuelzer after a review of several large series of cases in both age groups. The results demonstrated that whereas spontaneous recoveries occurred in 75 per cent of children, the same situation obtained in only 25 to 30 per cent of adults. In addition, whereas splenectomy was of benefit in two-thirds of the chronic cases in adults, the true value of the operation in children was still uncertain. In the acute type of ITP both sexes are affected with equal frequency while in the chronic type there is a definite preponderance of females. The experience in this clinic is in accord with the above observations and splenectomy has been performed in only 7 of the 31 cases with the diagnosis of ITP during the period of this study (1947 to 1953).

As the name implies, the etiology of ITP is still unknown. The association of ITP in children with concurrent or antecedent infection and with an allergic tendency is often stressed and Clement and Diamond have considered these factors of sufficient significance in their series to suggest that ITP may represent "a reaction to a bacterial antigen in a hypersensitive patient." Newton and Zuelzer, on the other hand, could not demonstrate a definite relationship between the occurrence of ITP and either infection or allergy. In adults there has been increasing evidence from the work of Harrington and associates and Stefanini and associates that ITP is based upon an immunologic mechanism, and antiplatelet substances have been demonstrated by in vivo and in vitro techniques. In children, however, platelet agglutinins have been demonstrated only rarely with the available techniques.

Cutaneous purpura constitutes the most common complaint in ITP and is often accompanied by epistaxis and bleeding from the oral mucous membranes. Relatively rare are the symptoms of hematuria, hematemesis, and melena. Central nervous system hemorrhage constitutes the most dangerous type of involvement but is, fortunately, rare. Physical examination, apart from evidences of hemorrhage, is generally unrevealing. Splenomegaly and lymphadenopathy are very uncommon in ITP and their presence requires that careful search be made for causes of secondary thrombocytopenic purpura such as leukemia, lymphoma, Gaucher's disease, and Still's disease.

Thrombocytopenia, with platelet counts usually below 60,000 to 70,000 per cubic millimeter, is the most significant finding on laboratory examination. This may be confirmed by the sparsity of platelets on blood smear where the relatively few platelets seen are often single, large, and abnormal in shape. In the presence of thrombocytopenia of sufficient degree to produce clinical purpura, it is usual to elicit prolongation of the bleeding time, increased capillary permeability on tourniquet test, and poor to absent clot retraction. The prothrombin and clotting times are normal. The existence of a true disturbance in the coagulation mechanism in ITP may be demonstrated, however, by the finding of defective prothrombin consumption. The latter determination was performed in Cases 4, 5, and 6 in the present series of patients with ITP and was found to be abnormal in each. A laboratory determination which promises to become of increasing importance is the investigation for the presence of antiplatelet agglutinins. This was not done on any patient in the present series. Bone marrow examination is important in order to rule out aplastic or neoplastic disease of the marrow which may cause purpura through destruction of the megakaryocytes. In ITP an increase in the number of megakaryocytes is usually seen; these are often abnormal in size, shape, and morphology and frequently do not appear to be forming platelets.

As indicated by recent investigations it appears likely that the spleen may be involved in one or more ways in the pathogenesis of

ITP. The spleen may be (1) one of the sites of production of antiplatelet agglutinins, (2) the site where antibody-affected platelets are removed, (3) the site of production of humoral factors which may have some relationship to capillary fragility as indicated by the fact that splenectomy often leads to lessening of hemorrhagic manifestations even in those cases in which platelet counts are not elevated after operation. These studies indicating that the spleen may be involved both in inhibiting platelet production and in promoting platelet destruction have reconciled earlier theories of Dameshek and of Doan.

For reasons discussed earlier, the indications for splenectomy in childhood are not definite. It seems clear, however, that a period of conservative management is indicated before operation is considered. The duration of this period differs among different groups of clinicians. With the majority of affected children demonstrating spontaneous recovery in 3 months, it would seem that this should be the minimum time for conservative observation. In the past, early splenectomy was generally considered advisable if severe and continued hemorrhagic manifestations were evident. Even this view has required modification following the demonstration that ACTH and cortisone may effectively control hemorrhagic manifestations even in those cases in which platelet response is not achieved by the therapy. Our own policy at present is to follow a conservative course for at least 3 months. This implies no therapy if purpura is mild, or the use of ACTH or cortisone if the bleeding is severe or persistent. In the absence of improvement in 3 months a course of 2 to 3 weeks of cortisone is given even to the mild cases in an attempt to achieve hematologic remission. With the persistence of thrombocytopenia after 6 months, splenectomy is considered. The exact time for operation varies with the age of the patient and with the severity of the hemorrhagic manifestations. Thus in mild cases conservative management may be continued for as long as 1 year while in severe cases and in girls approaching the menarche, operation is usually advised in 6 months. Persistent hemorrhage despite adequate therapy may require immediate splenectomy. It is possible that the detection of platelet agglutinins may delineate earlier those patients in whom splenectomy will be required. As mentioned earlier, platelet agglutinins have been found only rarely in children with acute ITP while very commonly in adults with the chronic type of the disease.

TABLE I.—IDIOPATHIC THROMBOCYTOPENIC PURPURA, RESULTS 1946 TO 1953

Case No. Patient Hospital No.	Duration of illness, mos.	Age at operation, yrs.	Platelet count		Duration of follow-up, mos.
			Preoperative, per c. mm.	Postoperative, per c. mm.	
1 M.K. 439195	1¾	3½	30,000	70,000	93
2 V.D. 537556	72	10½	40,000	360,000	58
3 F.C. 567431	12	10	60,000	210,000	45
4 L.L. 566845	18	11½	40,000	240,000	26
5 A.M. 591468	81	11	16,000	180,000	17
6 S.G. 659026	9	7	20,000	360,000	3
7 S.G. 663671	10	8½	20,000	430,000	5

The results of splenectomy in ITP during the period of study are shown in Table I. In 1 case (M.K.) the disease had existed for only 7 weeks, but operation was performed because of persistent purpura and epistaxis despite frequent transfusions. In this child splenectomy was a failure, the platelet counts returning to preoperative levels within 2 months following surgery. This patient was recently recalled and treated with oral cortisone. She demonstrated a striking response, with the platelets returning to normal levels in 1 week. Therapy was continued for 3 weeks but relapse occurred within 1 week after it was stopped. She subsequently responded to a second trial of cortisone which is being maintained at the present time. In the other 6 patients thrombocytopenia had been present for from 13 months to 6½ years. Two of the children had been given therapeutic courses of cortisone with no effect. In each of these

6 cases splenectomy has apparently resulted in cure. The period of follow-up has ranged from 3 to 58 months. Each of the 6 children has remained free of purpura and demonstrates normal platelet levels at present.

Because the value of hormone therapy is so impressive, we have adopted the following measures prior to operation. Significant deficiency in red cell volume is restored by whole blood transfusion. Two days prior to operation ACTH is started in therapeutic amounts and this is continued daily through the third to fourth postoperative day. This treatment results in control of hemorrhagic manifestations and serves to stimulate the adrenals of those patients who receive cortisone prior to operation. Two patients (Cases 5 and 6) were managed in this manner. Untoward effects have not been noted in the postoperative course and wound healing did not appear to be affected. There were no complications or deaths in the immediate postoperative period. Case 1 represents a late complication as noted earlier. The results of this series approximate those of other operative series in children.

The role of accessory spleens has been well presented by Curtis and associate and others. A histologically proved accessory spleen was found in 1 of our cases (Case 6). Case 1 is a possible candidate for reoperation. Elliot and Turner, however, failed to find retained splenic tissue by re-exploration in 2 patients with recurrence. They were unable to find retained accessory spleens in a third case at necropsy, wherein recurrence was the cause of death.

The result of operation is usually dramatic, but the "stress" effect of the operation may result in remission through hormonal mechanisms. Therefore, final evaluation should be delayed for at least 3 months.

The patient may obtain substantial benefit from splenectomy even in the absence of a rise in platelet count. Removal of the spleen may result in a cessation of bleeding manifestations in these patients, although a low platelet count persists.

HEREDITARY SPHEROCYTOSIS

This disorder is also known by the names congenital hemolytic jaundice, congenital hemolytic anemia, spherocytic anemia, chronic acholuric jaundice, and chronic familial jaundice. Because of the existence of cases demonstrating neither anemia nor jaundice, the designation of hereditary spherocytosis has been recommended.

Hereditary spherocytosis is a genetically determined disorder characterized by the production of structurally abnormal erythrocytes. The defect is transmitted, by either parent, as a mendelian dominant with the result that males and females are affected with equal frequency. The clinical manifestations may be extremely variable particularly as regards the time of onset and the intensity of symptoms. Thus the disease may be evident at birth in some instances while in others symptoms may not appear until late in adult life. Once symptoms appear, however, complete spontaneous remissions are very uncommon. Even in individual cases the manifestations may vary widely at different times in the course of the disease. Jaundice, symptoms referable to anemia, and splenomegaly constitute the most common clinical evidences of the disease. In children complaints of lassitude, fatigability, and poor skin color are frequently encountered. In the pediatric age group *acute crisis*, either as the presenting manifestation or as a complication of an established case, may appear at any time. These dramatic episodes are characterized by the sudden onset of fever, weakness, abdominal pain, nausea, vomiting, and a marked increase in pallor. Although these crises have generally been considered to result from a sudden acceleration in the rate of hemolysis, Owren has recently demonstrated, however, that at least some of the crises are due to acute aplasia of the erythroid elements in the marrow. There is some evidence that the "erythroblastopenic crises" may occur in the course of infection. Cholelithiasis is an extremely common occurrence in the course of untreated spherocytic anemia, having been found in 68 per cent of a large series of cases by Pemberton. In a recent study Young and associates (30) found gallstones in 12 of 14 patients with hereditary spherocytosis who were more than 11 years of age at the time of examination. Chronic leg ulcers, which have been reported in adults, are almost never seen in children. Roentgenologic changes are simi-

lar to those occurring in other congenital hemolytic syndromes and most commonly consist of thickening and striation of the frontal and parietal bones of the skull.

In the present group of 9 children, jaundice, of varying degree, was present in all. Crises occurred in 5 of the patients, in 4 of whom the episode constituted the first indication of the illness. In 2 of the patients who exhibited crisis, blood and bone-marrow studies revealed the erythroblastopenic type; in the other 3 patients clinical and laboratory evidence indicated accelerated hemolysis. Cholelithiasis was found in only 1 of the children, a 5 year old boy who developed common duct obstruction which required cholecystectomy. The biliary tract disease occurred 2 years prior to splenectomy, consent for which was persistently withheld by the mother. Following successful splenectomy upon the child, the mother consented to operation for herself, thus alleviating the jaundice and anemia from which she had suffered since early childhood.

It is of interest that in 4 of the children studied a family incidence of the disease could not be demonstrated. In each instance erythrocyte fragility studies and complete hematologic examinations were carried out on both parents of the affected child with negative results. In Cases 4 and 7 examination of 1 and 5 siblings respectively were also performed. Although none of the aforementioned techniques disclosed any abnormality, it is possible that additional diagnostic procedures, such as the determination of erythrocyte fragility on incubated blood may have revealed the trait in other members of the families. Even with the most complete diagnostic investigation, however, cases lacking family incidence have been reported. Then the possibility of gene mutation must be considered.

In hereditary spherocytosis the basic defect lies in the production of structurally abnormal erythrocytes. As a result of this red cell abnormality, an accelerated rate of red cell destruction takes place together with an increased rate of erythrocyte regeneration. The laboratory findings are explainable in terms of the following factors:

The structural defect in the erythrocyte is responsible for spherocytosis of the red cells on blood smear and increased osmotic and mechanical fragility of the red cells. The increased rate of red cell destruction produces anemia, hyperbilirubinemia, elevation of icterus index, increased fecal and urinary urobilinogen, and elevation of serum iron concentration. The increased rate of red cell regeneration leads to reticulocytosis, polychromasia of red cells on smear, appearance of normoblasts in peripheral blood, and erythroid hyperplasia of the marrow (except in aplastic crises). The Coombs test, which is commonly positive in "acquired hemolytic anemia," is almost always negative in hereditary spherocytosis.

All the children in the present study demonstrated frank spherocytosis, increased osmotic fragility of the red cells, anemia, reticulocytosis, hyperbilirubinemia, increased urinary urobilinogen, elevation of serum iron, and marrow erythroid hyperplasia. The Coombs test was negative in all instances. Mechanical fragility of the red cells and fecal urobilinogen excretion were not determined.

It has long been known that although splenectomy is followed by relief from all signs and symptoms of the disease and by disappearance of evidences of increased rates of erythrocyte destruction, the basic structural abnormality of the red cell persists. In recent years the role of the spleen in hereditary spherocytosis has been clarified greatly. Studies by Emerson and associates and by Young and co-workers have demonstrated that the spherocytes are more readily trapped in the spleen than are normal erythrocytes. The latter authors have also demonstrated that spherocytes may be trapped in the spleens of individuals suffering from disorders other than hereditary spherocytosis, thus tending to eliminate a specific abormality of the spleen itself as an integral part of the disease process. Evidence has been accumulated which indicates that stagnation of the spherocytes in the spleen results in lysis of some of the cells within the organ and in alteration of the trapped erythrocytes in such manner that they are more susceptible to destruction even after escaping from the spleen. Splenectomy removes the red cell "trap" with the result that the rate of hemolysis is sharply reduced.

TABLE II.—HEREDITARY SPHEROCYTOSIS, RESULTS 1946 TO 1953

Case No. Patient Hospital No.	Sex	Age at operation, yrs.	Average hgb. pre-operative, gm. per cent	Hgb. at present (gm.) per cent	Duration of follow-up, mos.
1 N.N. 539297	F	5½	8.3	13.0	51
2 B.D. 541279	F	13	10.9	14.1	35
3 T.D. 540510	M	10	10.3	13.6	35
4 L.A. 486881	F	9	9.7	14.5	30
5 P.L. 502939	M	4	7.4	15.1	21
6 R.L. 418057	M	7	9.2	14.8	18
7 A.S. 561619	F	13	8.0	15.3	17
8 R.D. 650173	M	5	9.3	12.0	11
9 T.C. 532995	M	4	6.9	13.3	17

In view of the universally excellent results from splenectomy together with the very high incidence of cholelithiasis in untreated cases, operation is indicated in every patient who gives clinical and laboratory evidence of an increased rate of red cell destruction. It should be emphasized that the absence of jaundice and anemia are not sufficient criteria for the diagnosis of a "latent case" or "spherocytic trait." Jaundice and bilirubinemia are largely dependent upon the excretory capacity of the liver; hemoglobin and red cell levels depend not only upon the rate of hemolysis but also upon the capacity for regeneration. Thus determination of fecal urobilinogen excretion may give evidence of a marked hemolytic disorder in the absence of jaundice or hyperbilirubinemia, while determination of the reticulocyte count may demonstrate accelerated red cell regeneration in the absence of anemia. In our own experience the age at which splenectomy is recommended has been decreasing steadily in recent years. The occurrence of cholelithiasis in a 5 year old child has prompted a reduction of the recommended age for splenectomy to between 3 and 4 years. With the excellent results reported by Gross in infants under 1 year of age, it is possible that operation is indicated in the first 2 years of life.

The role of transfusions in the therapy of congenital spherocytosis requires clarification. It has been suggested that transfusions be avoided because of the possibility that they may actually induce crisis. This has not occurred in our experience. Transfusions are indicated in crisis whether of the aplastic or hyperhemolytic type. Apart from crisis, transfusions are administered only when the hemoglobin concentration is at a sufficiently low level to produce symptoms of anemia in the patient. In preparation for surgery, however, deficits in blood volume are replaced by appropriate amounts of whole blood or packed red cells.

The results of operation listed in Table II were extremely gratifying in every case. Soon after splenectomy red cell and hemoglobin values rose to normal and have remained so in all cases. Jaundice, fatigability, and lassitude disappeared and a general improvement in activity and behavior was noted. A striking increase in appetite was frequently observed in the postoperative period and the children demonstrated a rapid weight gain in the early postsplenectomy months. In none of the children have any clinical or laboratory signs of a return of the disease process been noted. The period of follow-up has ranged from 11 to 51 months.

MEDITERRANEAN (COOLEY'S) ANEMIA

Cooley and his associates described an entity which they termed Mediterranean anemia, previously included in the von Jaksch's anemia group. This anemia is a congenital chronic hemolytic anemia with characteristic blood changes, increased resistance of the erythrocytes to hypotonic saline, and bone marrow hyperplasia. This anemia is further classified as trait, mild, moderate, and severe in this clinic. The large population of New York coming from Italian and Greek parentage has afforded this clinic a unique experience in the diagnosis and management

of Cooley's anemia. The majority of these patients have a Mediterranean heritage, but the report of 32 cases of this condition from Thailand and scattered reports from all over the world have diminished the importance of the geographic origin of these patients.

This condition is inherited as a dominant and both parents of a severely affected infant always show characteristic blood changes. A study of the close relatives of a suspected case thus contributes to the diagnosis. The individual with the trait or mild disease, who functions as a carrier, is regarded as heterozygous for a gene which, when homozygous, produces the severe disease.

While the mild form is asymptomatic and can only be detected by blood examination, the severely anemic patient presents a pathognomonic facial appearance. These features include prominent frontal and parietal bosses, enlargement of the head, prominent malar eminences, depression of the bridge of the nose, a mongoloid slant of the eyes, enlargement of the superior maxilla exposing the upper teeth, a muddy yellow complexion, especially noticeable in those receiving frequent transfusions, an icteric tint to the conjunctivae, small stature, and hypogonadism. The abdomen protrudes when splenomegaly becomes pronounced, especially in the younger child. The liver is also enlarged, but to a lesser degree. In persons with the moderate disease, the spleen may be slightly enlarged, and in the mild form not at all.

On laboratory examination increased resistance of red cells to hemolysis in hypotonic solutions of sodium chloride is found in all forms of Mediterranean anemia, mild and severe alike. In the trait and mild type, hypochromic macrocytes, microcytes, basophilic stippling, polycythemia, and target and oval cells are seen. The occurrence of morphologic changes far in excess of the degree of anemia characterizes the mild form. In the severe form very large thin hypochromic macrocytes (leptocytes) nucleated red blood cells, marked anisocytosis and poikilocytosis, and target and oval cells are found. The bone marrow in severe cases shows a predominance of nucleated red cells. Erythropoietic hyperplasia of a less marked degree is found in the mild or moderate forms. Roentgenographic changes are most common in the severe form, and these include osteoporosis, thinning of the cortex, trabecular atrophy, coarse reticulation, and thickening of the skull. Lateral views of the skull reveal an enlarged diploic space, which is either finely granular, mottled, or striated. Rarefaction characteristic of the disease in early childhood is replaced, with increasing age, by sclerosis in many areas of the skeleton, such as the tubular bones. The central portions of skeleton, skull, spine, and pelvic bones, however, retain the evidences of osteoporosis.

In addition to the structurally altered cell produced in patients with Mediterranean anemia, a variable percentage of the circulating hemoglobin is of the fetal variety. The amount of this type of hemoglobin present in the blood of a given patient is dependent upon the amount of transfusion therapy the patient has received. Transfusion has been shown by Smith and co-workers to depress hematopoiesis in these patients and thus decrease the percentage of fetal hemoglobin. The inherited defect is believed to be the inability to exchange to the synthesis of adult hemoglobin from the fetal variety following birth.

Lichtman and his co-workers have recently described an extracorpuscular defect in certain cases with the severe form of this illness. These workers found that the life span of transfused erythrocytes was diminished in these patients. They believed that this represented a form of "hypersplenism" and subjected this group of patients to splenectomy. The erythrocyte survival time returned to normal in all but 1 of these patients following operation. In addition to destroying red cells at an increased rate, the enlarged spleen may exert an inhibitory influence on the bone marrow. The large numbers of erythroblasts which appear in the blood following splenectomy support the latter theory.

A complication, which is assuming greater importance as patients with Mediterranean anemia are kept alive for longer periods of time, relates to the effects of iron overload. Increased iron deposited in the tissues of the patient with the severe disease results from the endogenous destruction of defective red cells, by the continuous increments derived

TABLE III.—MEDITERRANEAN (COOLEY'S) ANEMIA, RESULTS 1949 TO 1953

Case Patient Hospital No.	Age at operation, yrs.	Average hgb., gm. %		No. transfusions		Follow-up, mos.
		1 yr. preop.	Postop.	1 yr. preoperative	Postoperative†	
1 D.B. 370692*	6	7.5	8.4	39	24	14
2 S.S. 291967	11½	8.0	8.0	30	34	51
3 D.E. 516582	8	5.7	8.1	35	21	22
4 J.P. 222694	14	6.7	9.9	33	9	23
5 J.N. 404646	8	6.1	8.8	29	26	27
6 R.P. 161346	16	6.9	8.0	29	1*	18
7 M.G. 575818	3	6.6	8.2	28	5	11
8 F.G. 438307	8	6.4	8.0	27	11	11
9 A.D. 121407	17½	7.6	8.9	21	4	7
Combined Cooley's Anemia and Sickle Cell Anemia						
10 A.V. 426442	13½	6.8	8.5	30	12	34
11 F.P. 657406	14	9.2	11.5	6	0	3

*Patient died at another hospital from "encephalitis" 14 months after operation.
*Indicates blood given for study purposes only.
†Figures in this column represent the number of transfusions given during the *entire* follow-up period.

from transfusion and from accelerated absorption of this metal from the gastrointestinal tract. The iron introduced in this manner accumulates in the body and is not excreted so that in the course of many years, hemochromatosis frequently results. The length of time required for hemosiderosis to produce fibrotic changes characterizing hemochromatosis varies a great deal and depends on such factors as chronic anoxemia.

Three of the patients in this series (Cases 6, 10, and 11) developed extrahepatic biliary tract disease. Cholecystectomy and common duct exploration was performed 2 years prior to splenectomy in Case 6. A second patient (Case 10) developed acute cholecystitis 2 years after removal of the spleen and cholecystectomy was done. The third patient (Case 11) had cholelithiasis demonstrated by cholecystography prior to splenectomy and cholecystectomy is planned as an elective procedure.

These latter 2 patients (Cases 10 and 11) fall into a rare but interesting group: combined Mediterranean (Cooley's) anemia and sickle cell anemia. The Cooley's trait is inherited from one parent, the sickle cell trait from the other parent. This has usually been observed in Caucasians despite the fact that about 70 per cent of the hemoglobin in these patients is of the sickle cell form. This combination of factors in the same individual is elicited through hematologic studies of both the patient and the close relatives. The clinical manifestations consist of anemia and jaundice of varying intensity and moderate splenomegaly. The course of the 2 patients with the combined anemias differed somewhat from the patients having severe Mediterranean anemia alone. The onset of symptoms in the former patients was delayed and transfusions were not required until late in childhood. This is in sharp contrast to the patient with severe Cooley's anemia who may require transfusion before the first birthday.

Two of the 11 patients in this entire group demonstrated episodes similar to the aplastic crises described in hereditary spherocytosis. One of these patients (Case 5) with severe Mediterranean anemia sustained a sudden sharp fall in hemoglobin which was unattended by a rise in icterus or splenomegaly. The second patient (Case 11), who had the combined type of anemia, had frequent episodes similar to that described for the former case. In Case 5 the episode was accompanied by a concomitant purpuric eruption with a leucopenia and thrombocytopenia. Leucopenia and thrombocytopenia were also noted during this phase in the second patient. In both patients the episodes were of brief duration and the bone marrow returned rapidly to a hyperplastic state.

Penberthy and Cooley reported 5 cases in which splenectomy was performed for Mediterranean anemia. Operation was believed to make these children more comfortable and

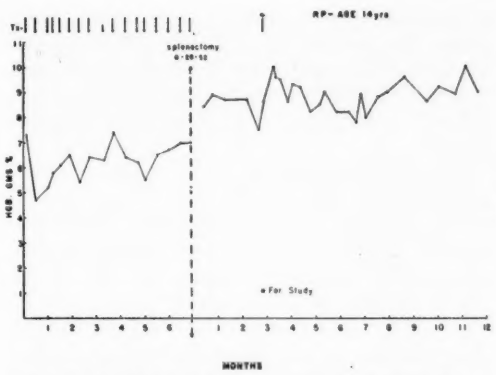

Fig. 1. Graphic representation of average hemoglobin level and number of transfusions (*Tx*) before and after operation in patient R.P. (NYH 161 346).

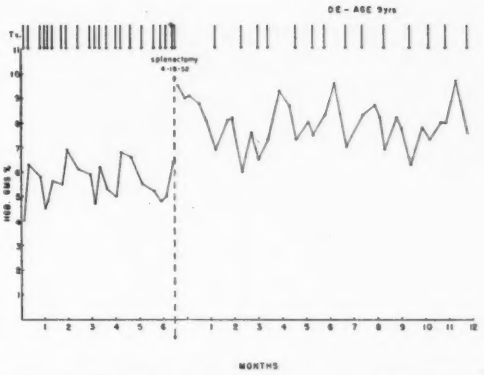

Fig. 2. Graphic demonstration of hemoglobin level before and after splenectomy in patient D.E. (NYH 16582). *Tx* indicates frequency of transfusion.

these authors thought that these patients lived slightly longer than the group not subjected to operation. Subsequent reports, however, have stated that splenectomy is contraindicated in this disease. It has been maintained that the spleen is a site of extramedullary hematopoiesis in such patients and is a necessary source of erythrocytes.

In our institution, two groups of patients with Cooley's anemia are considered as candidates for operation. One group of children with Mediterranean anemia develops progressive splenomegaly which may produce symptoms due to the size of the spleen and associated pressure on adjacent organ systems. Anorexia and inability to retain adequate amounts of food occur. This syndrome is believed to constitute an adequate indication in this group of children. The second group has been chosen because of a characteristic clinical course. Through repeated observation in the hematology clinic it was recognized that these patients could maintain a subnormal hemoglobin level (usually 7.0 gm. per cent) on a definite frequency of transfusion. In some of the patients the interval between transfusions had to be shortened to maintain their hemoglobin level. This condition was progressive and the patients eventually were unable to maintain an adequate hemoglobin level even on transfusions given twice a week. It was believed that this represented an increasing rate of hemolysis and splenectomy was planned for selected patients. The work of Lichtman and associates already reported demonstrated the hypersplenic component in these patients. Red cell survival studies by the Ashby technique should be utilized to estimate the degree of hypersplenism exhibited by a given patient. It is thought that this determination should be performed on all patients in whom splenectomy is considered for Mediterranean anemia.

There are certain other aspects of the management of these patients that are important. As these children approach adulthood every effort should be made to help the stabilization of their hematologic equilibrium. Thus, patients in their late adolescence should be studied carefully and splenectomy offered where it is believed that this may aid their management. As these patients survive to late adolescence their ability to synthesize hemoglobin should be determined. Transfusions are withheld as long as distressing symptoms remain absent and the patient's hemoglobin level is determined at frequent intervals. The minimum transfusions required to keep these patients comfortable should be found because of the inherent danger in transfusion therapy.

All of these patients received transfusions preoperatively to obtain the best level of hemoglobin prior to operation.

The results obtained in 11 patients subjected to splenectomy for Mediterranean anemia are listed in Table III. There were 5

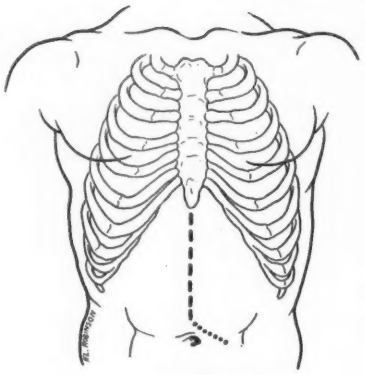

Fig. 3. The Bevan incision.

females and 6 males. The age of these patients varied from 3 to 17½ years at the time of splenectomy. Two cases of combined Cooley's anemia and sicklemia (Cases 10 and 11) are included. The management of these latter cases presents many of the problems that the management of Mediterranean anemia presents once the disease process has gathered momentum.

A histologically proved accessory spleen was found only in Case 3. There were no complications or deaths in the immediate postoperative period in this series. One late death occurred (Case 1) 14 months following splenectomy. This child died at another institution where he was admitted with the diagnosis of "encephalitis." Necropsy was not obtained.

Certain trends were noted in the follow-up of this group. In all of the patients in this series the average hemoglobin level was elevated in comparison to the average before operation. This observation is particularly significant when considered with the fact that the number of transfusions was decreased in each instance. These observations are shown graphically in Figures 1 and 2 which represent the best and worst results in this series. One patient (Case 6) has received only 1 transfusion since the operation and that was given for study purposes. The difference in response of the individual patient remains obscure. The various factors are under scrutiny and may appear as experience increases in this clinic. It has been our impression that the patient who is subjected to operation after puberty receives the greatest benefit from splenectomy. However, the variability of the degree of anemia within the "severe" group must be considered in evaluation of response to splenectomy.

Despite the short period of follow-up, certain late developments have been observed in these patients. A demonstration of the increased load thrown on the bone marrow was observed in 2 patients (Cases 4 and 9). These patients developed severe bone pain, particularly in the lower extremities when transfusions had been withheld for long periods. These symptoms promptly disappeared when transfusions were given in the absence of severe anemia. The genesis of this pain appeared to be related to the hyperfunction of the bone marrow in these patients.

A serious late complication was seen in 4 of these patients (Cases 3, 5, 9, and 10) who suddenly developed acute pericarditis which appeared life-threatening in 3 cases, but caused only vague pain and discomfort in 1 patient. Despite careful study in these cases the etiology was not demonstrated. The course of this illness appeared self-limited and these patients responded to symptomatic therapy.

Recent reports of operative results in this condition have been more optimistic. This development has resulted undoubtedly from a clarification of the spleen's part in the pathologic process and the understanding of the place of splenectomy in the management of this disease. Splenectomy in the experience of this clinic has a definite place in the management of selected cases of Mediterranean anemia. It eases the burden of therapy in these children by decreasing the number of transfusions they require. The increased hemoglobin level benefits the entire organism. It must be stressed, however, that splenectomy is only palliative. The basic defect in blood formation still remains in the affected individuals.

TECHNICAL CONSIDERATIONS

Preoperative preparation of patients coming to splenectomy is of importance. As already noted any blood volume deficit should be corrected to as near normal as possible by

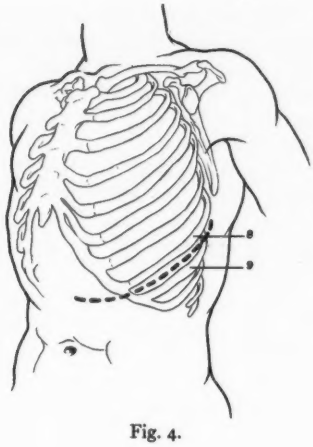

Fig. 4.

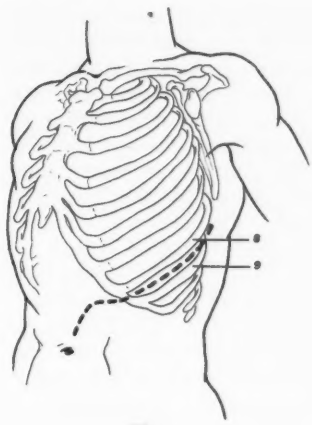

Fig. 5.

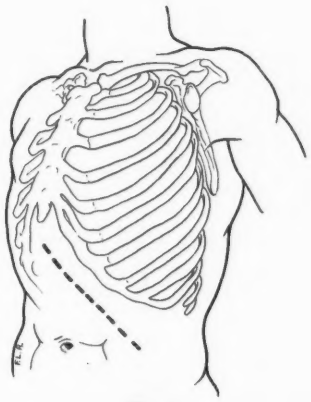

Fig. 6.

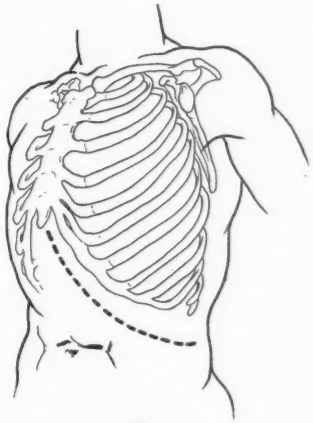

Fig. 7.

Fig. 4. Transthoracic incision recommended by Carter.
Fig. 5. Transthoracic incision reported by Humphreys.
Fig. 6. The incision recommended by Singleton.
Fig. 7. Modification of the Singleton incision as used in the author's clinic.

the transfusion of whole blood or packed red cells as indicated by the patient's laboratory findings. These patients are kept on nothing by mouth for at least 6 hours prior to operation, and to insure further complete decompression of the stomach an indwelling nasogastric tube is placed an hour before the anesthesia is begun. An empty stomach facilitates exposure of the spleen during the operative procedure.

In very young children in whom venipuncture for infusion or transfusion purposes is difficult, it is our practice to place a small polyethylene catheter in a vein under direct vision the night before the procedure.

The choice of the anesthetic agent in children suffering from idiopathic thrombocytopenic purpura and hereditary spherocytosis depends in large part on the associated conditions which the patient may have. Frequently, children with Cooley's anemia may show slight liver dysfunction with the routine liver function tests. We have used ether anesthesia in these children largely for this reason. It is

recommended that anesthesia be administered via an endotracheal closed system to patients undergoing splenectomy. Small transpleural perforation may occur during dissection of the spleen from the diaphragm and may pass unnoticed by the operator. Positive pressure applied to such a closed system prior to closure will bring such perforations to the attention of the surgeon, and aid in preventing the complications associated with a collapsed lung.

Longitudinal incisions enjoy widespread use in the literature and have been described by Bevan, Wilkie, and Andrus. The Bevan incision is demonstrated in Figure 3. This incision provides good exposure of the splenic vessels, but the spleen must be separated from its bed by blind dissection with its associated hazards.

More recently, with the advance of thoracic surgical technique, transthoracic and combined thoracoabdominal incisions have been proposed. These incisions have been reviewed by Carter (Fig. 4), Humphreys (Fig. 5), and by Burke and Jacobs, and Hart. This type of approach gives excellent exposure to the diaphragmatic and lateral surfaces of the spleen. Vascular channels in adhesions between the spleen and surrounding viscera are most commonly encountered in these areas, and this incision has been suggested to permit dissection under direct vision. We are loath to use this incision in children because of the added trauma and possible morbidity of complications associated with a combined incision. We have yet to encounter a spleen in this age group of sufficient size to make its removal by such an incision mandatory. Madden and Applebury reported the removal of a very large spleen (5,450 gm.) through a paramedian incision.

In our hands a modification of the oblique incision recommended by Singleton (Fig. 6) has been successfully employed in the majority of the reported series. The patient is placed in the supine position with the patient's left shoulder elevated slightly by support. The incision is started from the left of the xiphoid process and is carried down in curvilinear fashion to the posterior axillary line, roughly paralleling the costal margin (Fig. 7). The rectus muscle, where encountered, is transected in this same incisional line, the external oblique muscle is split in the direction of its fibers, and the posterior rectus sheath and transverse muscle are transected. The peritoneum is then opened with care. Exposure is excellent and any adhesions between the spleen and surrounding surfaces are easily divided under direct vision by sharp dissection. This step is aided by gentle traction on this organ. All vessels encountered are clamped before transection.

The next step is to mobilize the spleen through an incision in the lateral peritoneal reflection of the spleen. As pointed out by Wilkie, the "fascia propria" underlies the peritoneum and must be transected before the spleen can be mobilized with ease. As the organ is carefully rotated medially the pedicle together with the tail of the pancreas is readily recognized. The splenic pedicle is then gently dissected from the latter structure. It is preferable to ligate and transfix the vessels individually and secure the arterial supply first. When the spleen is excessive in size or it becomes apparent that the posterior approach is not feasible, the branches of the splenic artery near the hilum may be individually clamped and ligated with the accompanying veins. With gentle traction the gastrosplenic omentum may be tensed and the individual vasa brevia isolated, clamped, and ligated. Careful inspection of the bed of the spleen is necessary to insure complete hemostasis. The abdomen is then closed in layers without drainage. Care is taken to re-establish the normal anatomic relationships of the abdominal wall. The use of this technique in removing the spleen in children has been quite satisfactory in our experience. In no child in this entire reported series of cases were any technical problems of note encountered. The use of the subcostal incision has enabled the operator to remove the organ easily even when the spleen extended well into the pelvis. Splenomegaly of this degree was encountered regularly in the Cooley's anemia group.

Following operation these patients are kept on intragastric decompression for 24 to 48 hours depending upon the appearance of bowel activity. They are then started on oral feeding and progressed in their diet as they

tolerate it. In cases in which transthoracic procedures have been done it is the practice in this clinic to close the chest without drainage. Portable roentgenography of the chest is utilized to determine if residual pneumothorax exists in the period following operation.

These patients are ambulated with supervision on the first postoperative day unless there is some contraindication.

It should be emphasized that platelet counts should be done on these patients postoperatively and the peripheral platelet level followed closely. The experience in this group of patients indicates that the platelet rise following splenectomy does not follow a general pattern. In this clinic a platelet count of 1,000,000 per cubic millimeter has been taken arbitrarily as the indication to start anticoagulant therapy. Two of the children in the purpura group (Cases 5 and 6) and 1 patient having combined sicklemia and Mediterranean anemia received anticoagulant therapy in their postoperative periods. This precaution, we believe, prevents the distressing complication of portal thrombosis, which may occur following removal of the spleen.

As indicated previously, follow-up of these patients after discharge is mandatory. This is especially true in the Mediterranean anemia group where close supervision is necessary until hematopoietic equilibrium is reached.

SUMMARY

1. Splenectomy was performed on 9 children with hereditary spherocytosis, 7 with idiopathic thrombocytopenic purpura, 9 with severe Mediterranean anemia, and 2 with combined Mediterranean anemia—sickle-cell disease.

2. Clinical and laboratory features of the various diseases were summarized.

3. Current concepts of the role of the spleen in each disorder were reviewed.

4. The indications for and the results of splenectomy in this group of hematologic disorders in children were presented.

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EQUILIBRATION TIME OF WATER (DEUTERIUM OXIDE) FOLLOWING INTRAVENOUS INJECTION IN THE BATTLE CASUALTY

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THE present study of the equilibration time of water (deuterium oxide) following intravenous injection was part of a broad survey of the systemic response to injury carried out by the Surgical Research Team on the Eastern Front in Korea during 1952 and 1953. The response to severe injury appears to be a response of every organ, every system, and presumably every cell in the body. This response to injury is not a response of a few hours but is a response of days or weeks in duration.

Following its intravenous injection in the normal subject, deuterium oxide diffuses very rapidly throughout the total body water. Equilibration was found by Schloerb and associates to be quite rapid and to be complete within 2 hours.

This rate of diffusion may well be a measure of the efficiency of the "total circulation" of the body. It measures the overall efficiency of the mixing within the blood stream, delivery to various parts of the body, diffusion into extracellular and intracellular fluid, secretion into the gastrointestinal tract and finally equilibration. It is thus a measurement of the efficiency of the overall circulation, for in this broader sense the status of the circulation may be assayed as to its efficiency in taking substances from one fluid compartment or from one cell to another across several membranes and across several fluid compartments. Thus, for example, the circulation must move oxygen from the pulmonary alveoli to the muscles of the leg and metabolites from the cells of the leg to the cells of the liver, kidneys, or lungs across several fluid compartments. This function cannot be evaluated by measurements of blood pressure, blood volume, cardiac output, or peripheral resistance. The equilibration rate of intravenously injected deuterium oxide offers a means of testing this function.

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MATERIAL AND METHODS

The study was done in a forward surgical hospital in Korea. Deuterium oxide (99.8 per cent pure) was prepared as an isotonic solution of sodium chloride.

The injection was made by syringe and required approximately 1 minute.

Venous samples were then taken from the opposite arm at stated periods of time. The plasma was separated, placed in a sealed glass test tube and shipped via air to the Bureau of Standards for analysis of deuterium content by a method which has been previously described (1).

Five battle casualties and 2 normal subjects were studied.

OBSERVATIONS

Normal subjects. Two normal male subjects were studied; one 32 years of age (Fig. 1), the other 20 years of age (Fig. 2). Each was given 50 grams of deuterium oxide in the antecubital vein. Serial studies were then made of the concentration of deuterium in the plasma obtained from the antecubital vein of the opposite arm.

Patient No. 1. This 22 year old soldier was injured 6 hours prior to admission to the forward hospital. His injury, inflicted by small arms fire consisted of a penetrating wound of the arm. Arterial bleeding was controlled by ligation of a small vessel. The radial pulse was palpable. His blood pressure was 60/20, pulse 120 per minute. After a transfusion of 500 milliliters of blood, his blood pressure was 80/50. He was then given a rapid injection of deuterium oxide (50 grams) intravenously.

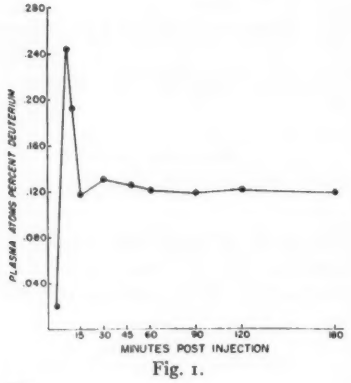
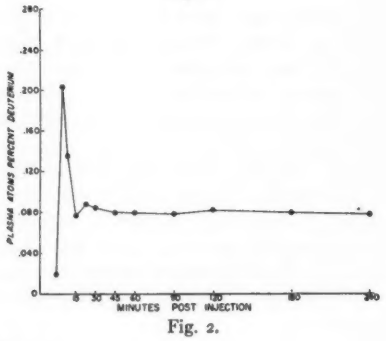


Fig. 1.



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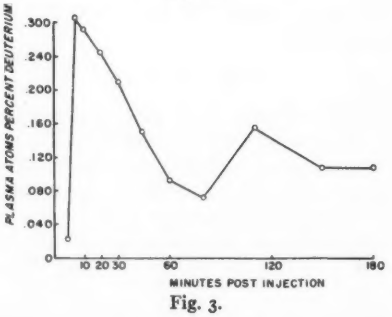


Fig. 3.

Sixty minutes later transfusion was again started as a slow drip. His subsequent course was smooth. His plasma volume (T-1824 method) indicated a deficiency of 23 per cent from the normal volume calculated as 45 milliliters per kilogram of body weight. All studies of deuterium concentration were made from venous plasma from the arm opposite the one used for the infusion of deuterium oxide and blood.

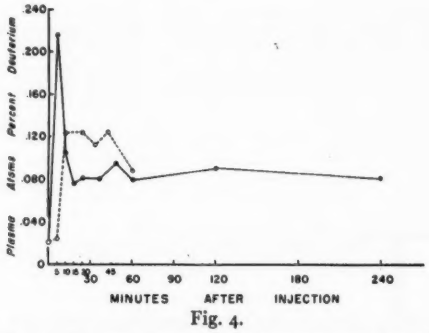


Fig. 4.

Fig. 1. Venous plasma deuterium concentration after intravenous injection of deuterium oxide in normal subject. Equilibration is very rapid and has occurred within 60 minutes.

Fig 2. Venous plasma deuterium concentration after intravenous injection of deuterium oxide in normal subject. Equilibration has probably occurred within 45 minutes.

Fig. 3. Venous plasma deuterium concentration after intravenous injection of deuterium oxide in patient No. 1. The period of initial elevation of plasma deuterium concentration is quite prolonged and probably indicates the reduction in capillary profusion.

Fig. 4. Venous plasma and deuterium concentration after intravenous injection of 50 grams of deuterium oxide in patient No. 2. Equilibration time appears essentially normal. The gastric deuterium concentration was high immediately after injection and was slow to equilibrate with the venous concentration.

The results of this study are shown in Figure 3.

Patient No. 2. This 31 year old American soldier was admitted to the forward hospital 5 hours after injury. The wound, produced by artillery shell fragments, consisted of a penetrating wound of the chest, diaphragm, and liver. Laparotomy under pentothal, nitrous oxide, and ether anesthesia permitted drainage of the small hepatic wound. His subsequent course was very smooth.

On the first day after injury, his plasma volume measurement demonstrated a deficit of 12 per cent but he appeared in excellent condition. His vital signs were normal. At this time he was given 50 grams of deuterium oxide intravenously (Fig. 4). His course remained uneventful.

Patient No. 3. This 20 year old Korean soldier was injured by mortar shell fragments. The wounds included a perforation of the transverse colon and a penetration of the face. He was slightly hypotensive (blood pressure 100/70), on admission to the hospital.

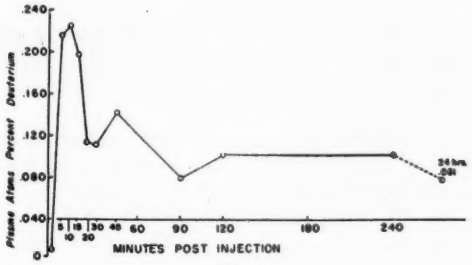
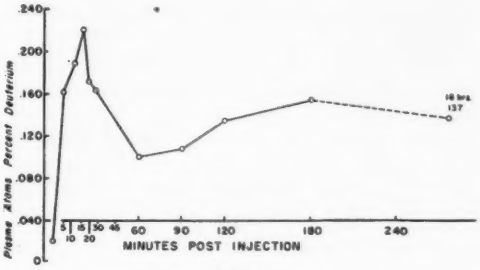


Fig. 5.



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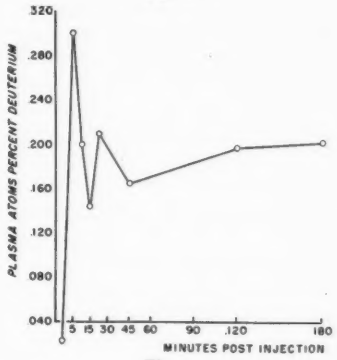

Fig. 7.

Fig. 5. Venous plasma deuterium concentration after intravenous injection of 50 grams of deuterium oxide in patient No. 3. The initial rise in concentration is more pronounced and prolonged than in the previous patient. Equilibration again occurred within 2 hours.

Fig. 6. Venous plasma deuterium concentration after intravenous injection of deuterium oxide in patient No. 4 5 days post injury. Equilibration did not occur within 2 hours. The initial peak in concentration persists for a prolonged period. These two observations probably result from the marked plasma volume deficiency and the poor circulation in the left leg.

Fig. 7. Venous plasma deuterium concentration after intravenous injection of deuterium oxide in patient No. 5. Equilibration has occurred more rapidly and the initial peak in the curve was of shorter duration than in the more severely injured twin. Within the limits of the method, equilibration appears to have been completed within 120 minutes.

After a transfusion of 1,000 milliliters of blood, colostomy was performed under pentothal, nitrous oxide, and ether anesthesia. His subsequent course was smooth.

On the second day after injury, his plasma volume deficit was 10 per cent. He was, at this time, given 50 grams of deuterium oxide intravenously (Fig. 5). His blood pressure was 110/75, pulse rate 80, and pulse volume full.

Patients Nos. 4 and 5. These patients were identical twins and were injured on March 2, 1952, by fragments of the same exploding shell. They were admitted to the forward surgical hospital 6 hours after injury.

Patient No. 4 was admitted in a state of incipient shock. His injuries included soft tissue wounds of 3 extremities. The left femoral artery and vein had been severed and were ligated. The foot became cold and pale and was without a detectable pulse. The capillary circulation was decreased as indicated by a delayed return of color following release of pressure on the skin. Edema was marked. Only after a lapse of several days was the survival of the leg assured.

His postoperative plasma volume determination indicated a deficiency of 24 per cent.

Patient No. 5 had 3 small wounds of the face and extremities. Débridement was a minor surgical procedure. He was ambulatory immediately after operation. His plasma volume determination showed a normal volume.

Each patient was given 100 grams of deuterium oxide 5 days after injury (Figs. 6 and 7).

DISCUSSION

Following the intravenous injection of 50 grams of deuterium oxide into the 2 normal subjects, a similar equilibration pattern evolved. The venous concentration of deuterium rose sharply but fell immediately so that 15 minutes after the injection the plasma concentration had fallen to reach a level approximating the concentration of equilibration (Figs. 1 and 2). In both subjects, this initial period of elevation was 15 minutes or less in duration. After minor changes in con-

centration, equilibration was complete within 60 minutes.

Patient No. 1, who was in a state of moderate hypotension due to blood volume deficiency, demonstrated a sharp rise in deuterium concentration which slowly subsided over a period of 80 minutes. Equilibration was apparently reached after 150 minutes (Fig. 3). This prolonged period of equilibration may well be the result of blood volume deficiency and vasoconstriction. A reduction in the active capillary bed would decrease the rate diffusion from the blood to the extravascular fluid compartments. Arteriovenous shunts could result in such a prolonged equilibration time.

Patient No. 3 required 120 minutes to equilibrate on the second day after perforation of the colon. This deficiency may represent in part, the effect of the initial injury and, in part, the effect of the continuing nature of the injury in the form of peritonitis.

Patients Nos. 4 and 5, being identical twins, differed only in the magnitude and nature of their wounds. Patient No. 4 was severely injured and had one extremity with a very limited circulation. His equilibration curve was very similar to that of Patient No. 1 who was hypotensive from blood loss. In contradistinction, Patient No. 5 had an elevated deuterium concentration for only 15 minutes, although he did not equilibrate within the first hour. Thus anesthesia and minor injuries affected his circulatory efficiency to a minor degree for a period of at least 5 days.

SUMMARY

1. The equilibration time and pattern of intravenously injected deuterium oxide offers a test of function of the circulation following injury.

2. Equilibration in 2 normal subjects was almost complete within 15 minutes and was apparently complete within 60 minutes.

3. The hypotensive state following hemorrhage was associated in 1 patient with a prolonged equilibration time.

4. Severe injury followed by anesthesia was associated with a prolonged deficiency in the circulation as indicated by a prolonged equilibration time of deuterium oxide.

CONCLUSIONS

Following severe injuries, the deficiency in the "total body circulation" is quite marked. This deficiency may persist for several days in spite of an apparently smooth convalescence. This defect is presumably due to oligemia and vasoconstriction but this has not been proved.

The response of the circulatory system to trauma, like the response of every other system in the body, appears to be of considerable magnitude over a long period of time.

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INFLUENCE OF PARTIAL AND COMPLETE EVISCERATION ON THE ACTION OF DRUGS PROTECTING AGAINST LETHAL HEMORRHAGE

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THE progressive sequestration of blood within the abdominal viscera during hemorrhagic shock would seem to represent the critical defect which precipitates circulatory collapse and is responsible for the ultimate ineffectiveness of blood replacement measures. There is, however, no agreement as to the factors responsible for the decompensatory tendency during this phase of the syndrome. At least two separate sequelae of protracted hypotension have been implicated—impairment of peripheral vascular regulatory mechanisms within the liver and gastrointestinal tract through the local effects of stagnant hypoxia, and the systemic dissemination via the bloodstream of deleterious vasoactive principles from these areas.

Pretreatment with a number of pharmacologic agents or with particular antibiotics has been shown to attenuate the lethal character of the shock syndrome. Information concerning the precise mode and site of action of such protective agents, in conjunction with organ ablation experiments, would appear to offer a reasonable approach toward the clarification of this problem. For this purpose, use was made of the procedure developed by Engel and co-workers in which the intestinal tract and/or the liver in the rat could be surgically removed to provide a viable experimental animal.

The present experiments in the rat indicate that evisceration almost completely abolishes the progressive decompensatory pooling of blood during the latter stages of hemorrhagic hypotension. They also indicate that the protective action of two agents, dibenzyline[1] and chlorpromazine[2] would appear to reside in different mechanisms, since dibenzyline was found to be protective only in the presence of the liver, while chlorpromazine was effective even when both the liver and gastrointestinal tract had been surgically removed.

MATERIAL AND METHODS

Three groups of animals were subjected to graded hemorrhage: (a) normal controls; (b) eviscerated rats (involving removal of gastrointestinal tract, pancreas, and spleen, and tying off the circulation to the liver); (c) partially eviscerated animals (with the blood supply to the liver via the hepatic artery intact).

The inferior mesenteric, superior mesenteric, and celiac arteries were ligated in that sequence. The bowel was separated at the rectum and the intestinal tract reflected back to one side. After the spleen had been removed, the stomach was separated from the esophagus close to the diaphragm, the portal vein was ligated and severed, and the entire visceral mass removed. The isolated liver was left in situ. A comparable series of experiments was carried out in which the hepatic artery was dissected free and left intact to provide a circulation through the liver. These will be referred to as H.A. preparations. In all experiments, the visceral mass was weighed and taken into account in computing total blood loss. Following closure of the abdominal incision, the left carotid artery was cannulated for blood pressure recording and hemorrhage. The entire procedure required from 20 to 30 minutes.

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This work was supported in part by a research grant (H-1244) from the National Heart Institute of the National Institutes of Health, United States Public Health Service, and by a grant from the Life Insurance Medical Research Fund.

Dr. Kelan is now located at the University of Indonesia Medical School, Djakarta, Indonesia.

[1] N-phenoxyisopropyl-N-benzyl-β-chlorethylamine hydrochloride.

[2] SKF 2601-A "thorazine," 10-(γ-dimethyl amino-propyl)—2—chlorophenothiazine hydrochloride.

TABLE I.—BLOOD LOSS DURING HEMORRHAGIC HYPOTENSION

Category	Normal			Eviscerate			Hepatic artery preparation		
	No. rats	Max. loss per cent	Uptake per cent	No. rats	Max. loss per cent	Uptake per cent	No. rats	Max. loss per cent	Uptake per cent
No treatment	10	3.89	1.13	10	2.93	0.36	8	3.1	0.67
Dibenzyline	4	3.23	1.27	6	2.82	0.37	6	2.9	0.65
Chlorpromazine	8	3.85	0.74	12	2.5	0.66	11	3.1	0.78

Dibenzyline—20 μgm./100 gm.; chlorpromazine—2.5 mgm./100 gm.

In order to rule out the drug action of different anesthetic agents, the experiments were performed during three types of anesthesia: sodium pentobarbital (3.5 mgm./100 gm.) was given intramuscularly, ether by the open drop method, and a mixture of trichlorethylene and nitrous oxide-oxygen using a new rat anesthetizer developed by Hershey. In each case, an attempt was made to maintain the animals at equivalent depths of anesthesia. Although the entire experiment encompassed 4 hours, no additional anesthesia was required after the surgery had been completed and the blood pressure had been reduced to shock levels.

In this regard, mention should be made of the effects of chlorpromazine in relation to anesthesia. The drug in high doses has been shown by Courvoisier and associates to afford a degree of narcosis. When used alone, in the dose employed (2.5 mgm./100 gm.) in the present studies, chlorpromazine had only a moderate narcotizing effect. However, the agent potentiates the action of many anesthetic drugs, so that smaller doses of the latter suffice to provide surgical anesthesia. For example, with sodium pentobarbital, only 2.0 to 2.5 milligrams were required to produce surgical anesthesia in rats receiving chlorpromazine (2.5 mgm./100 gm.).

Following eviscération, recovery from anesthesia had advanced sufficiently for the rats to react to painful flexure of the joints or pinching of the tail. Blood pressure readings averaged between 110 and 140 millimeters of mercury. Occasionally, because of the accidental blood loss during the surgery, animals were found to have blood pressures below 100 millimeters of mercury. These were discarded and not used for the subsequent hemorrhage experiments.

In most instances, hemorrhage was begun within 10 to 15 minutes after eviscération. The procedure was designed to provide a uniformly lethal type of shock by graded bleedings at 5 minute intervals until the blood pressure had fallen to and remained at 35 to 40 millimeters of mercury. Bleeding was carried out through a glass cannula in the carotid artery into a 10 milliliter volumetric pipette which served as a reservoir. The blood was heparinized and allowed to collect in the lower of two volumetric pipettes, arranged in series as an automatic transfusion device to maintain the pressure at a desired level, as described by Baez and associates. An attempt was made to sustain the animals at this level of hypotension for 3 hours. Animals surviving beyond that time were infused with the blood remaining in the reservoir and all open wounds closed. Because of the multiplicity of factors which influence the long range recovery of eviscerated animals, the survival statistics are based on a 4 to 5 hour period subsequent to blood replacement.

The protective action of two drugs was investigated. Dibenzyline (20 μgm./100 gm.) or chlorpromazine (2.5 mgm./100 gm.) was given intramuscularly 15 to 20 minutes before the induction of anesthesia.

EXPERIMENTAL FINDINGS

Effects of surgical eviscération. No supportive measures were taken to prolong the life of eviscerated rats in order to avoid the introduction of features which would complicate the interpretation of the experimental findings. Completely eviscerated rats, especially after inhalation anesthesia, remained alert and showed no evidence of deterioration for at least 6 to 8 hours, well beyond the 3 to 4 hour

period of experimental procedure. Such animals, when subjected to a sham procedure in which the carotid artery was cannulated and blood pressure recorded for 4 hours, continued to maintain a normal blood pressure level throughout. Rats, in which only partial evisceration was performed, with the hepatic artery (H.A.) to the liver intact, survived for more than 24 hours up to periods of 36 hours.

Tolerance to hemorrhage. Almost identical patterns of response were obtained with the three anesthetic procedures employed, when comparable depths of anesthesia were maintained. No significant benefit of any given anesthetic procedure was observed, although with the inhalation anesthetics a somewhat greater blood loss was required to achieve standard hypotensive levels.

Control rats, subjected to a standard graded hemorrhage, required on the average the removal of 3.9 per cent of body weight of blood to maintain the animal in a state of drastic hypotension (35 mm. Hg for 3 hours, Fig. 1). It was found that eviscerated rats would not tolerate a blood pressure level of 35 millimeters of mercury for longer than 10 to 20 minutes. These experiments were, therefore, carried out at 40 millimeters of mercury, a level which, although uniformly lethal was more amenable to blood loss and statistical evaluation. Eviscerated rats tolerated a maximum blood loss of from 2.5 to 2.9 per cent of body weight (Table I). Presumably this reduced tolerance to bleeding was a reflection of the volume of blood removed in the surgically extirpated organs. Partially eviscerated rats (H.A. intact) showed blood loss values surprisingly close to those of unoperated upon controls. It is of interest that pretreatment with either dibenzyline or chlorpromazine had no significant effect on the maximal blood loss achieved, despite their protective action.

With the induction of drastic hypotension, decompensation sets in, necessitating blood replacement to maintain the pressure at 35 to 40 millimeters of mercury. This was reflected in the spontaneous uptake of blood from the bleed-out reservoir. Control rats took up (on the average) about 29 per cent of the total blood lost during the 3 hour hypotensive episode. In sharp contrast, eviscerated rats

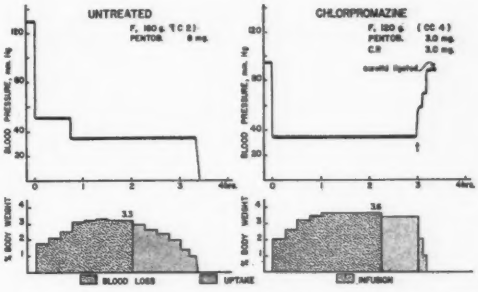

Fig. 1. Two protocols comparing the response of normal rats subjected to hemorrhage with and without drug treatment. The protective action of chlorpromazine (c.p.—2.5 mgm./100 gm.) is readily apparent, rat CC 4 being sacrificed 12 hours later. Note considerable reduction of "uptake" from reservoir after treatment with chlorpromazine.

showed a lesser uptake tendency (13 per cent) and usually collapsed suddenly during the second hour of hypotension (Fig. 2). More than half of these animals died without appreciable take-up of blood. Death appeared to be the result of an acute respiratory failure and subsequent cardiac embarrassment.

In order to rule out the possibility that the sudden collapse was not the consequence of respiratory obstruction, a small bore plastic catheter was inserted into the trachea. Aspiration through this catheter was frequently performed to prevent the accumulation of mucus. The results were identical with the previous findings. Blood replacement had no sustained supportive effect at this stage.

In experiments with partially eviscerated rats (H.A. intact), it was found that the maintenance of blood pressure at 40 millimeters of mercury, as employed routinely in the completely eviscerated preparation, was well tolerated for 3 hours, with only minimal uptake of blood. In this respect, H.A. preparations behaved as well as normal controls, and were definitely superior to completely eviscerated rats. In order to study the possible protective action of dibenzyline and chlorpromazine, a more drastic procedure was employed in which the blood pressure level was lowered to 35 millimeters of mercury and maintained up to 3 hours. Under these conditions, the partially eviscerated animal (H.A. preparations) showed a more pronounced tendency for uptake of blood (21 per cent).

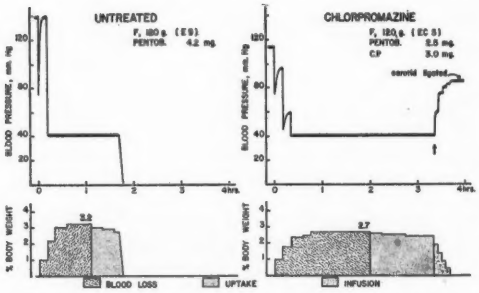

Fig. 2. Protection afforded by chlorpromazine (c.p.—2.5 mgm./100 gm.) in completely eviscerated animals subjected to hemorrhage. Note minor "uptake" of blood in absence of viscera. No significant differences in blood loss values of protected rat (EC 5) and untreated rat (E 9).

Despite this, circulatory collapse did not develop until somewhat later than in completely eviscerated cases, usually during the third hour of hypotension (Fig. 3).

Pretreatment with dibenzyline had no significant effect on the uptake phenomenon even in normal rats where protection was afforded (Table I). Chlorpromazine, on the other hand, definitely diminished the tendency for uptake of blood in control animals. Furthermore, in eviscerated rats, chlorpromazine permitted the tolerance of 3 hours of hypotension, with a total uptake only slightly greater than that exhibited by untreated counterparts during only a 90 minute period at 35 to 40 millimeters of mercury (Fig. 2).

TABLE II.—SURVIVAL FOLLOWING GRADED HEMORRHAGE

	No. rats	No anesthesia	Pento-barbital	Ether	Trilene-N_2O
Normal controls Untreated	10	—	1/5†	0/1	0/1
Dibenzyline	4	—	2/2	1/1	1/1
Chlorpromazine	8	2/2	4/4	1/1	1/1
Eviscerate rats Untreated	10	—	0/7	0/2	0/1
Dibenzyline	6	—	0/2	0/3	0/1
Chlorpromazine	12	2/2	7/7	2/2	1/1
Partial evisceration (H.A. intact) Untreated	8	—	1/5	0/2	0/1
Dibenzyline	6	—	3/3	2/2	1/1
Chlorpromazine	11	3/3	4/4	3/3	1/1

Survival based on number of animals alive 3 to 4 hours after blood replacement.

†Fraction represents number of survivors as numerator, in relation to total number of cases as denominator.

Dosage of dibenzyline, 20 μgm./100 gm.—chlorpromazine, 2.5 mgm./100 gm. in anesthetized rats; 5.0 mgm./100 gm. in cases in which chlorpromazine alone was used.

Effect of drugs on survival following graded hemorrhage. With the procedure employed, 80 per cent of the control rats subjected to hemorrhage succumbed either immediately or shortly after blood replacement (Table II). In direct contrast, rats receiving dibenzyline or chlorpromazine prior to hemorrhage showed a 100 per cent recovery.

As indicated in the accompanying protocol (Fig. 2), completely eviscerated rats succumbed readily to a hypotension of 40 millimeters of mercury. Administration of dibenzyline, in doses which had been found to protect against the lethal outcome of hemorrhage in controls, had no beneficial influence on the response of the eviscerated animal. Chlorpromazine, on the other hand, had a clearcut restorative action on the capacity of these rats to withstand hemorrhagic hypotension (Fig. 2). Respiration remained deep and more regular following blood loss. The pulse pressure continued to be clearly evident throughout the period of hypotension. No hypoxic changes could be detected in the carotid blood in the glass arterial cannula. Furthermore, instead of sinking into a comatose state following hemorrhage, eviscerated rats treated with chlorpromazine continued to respond to painful stimuli throughout. The blood pressure response to blood replacement was rapid and sustained. As indicated in Table II, 100 per cent of these rats recovered in contrast to the uniformly lethal outcome in untreated animals and those given dibenzyline.

Although rats subjected to partial evisceration (H.A. intact) tolerated blood loss better than completely eviscerated animals, only 12.5 per cent survived following blood replacement (7 out of 8 collapsing before the end of the 3 hour period of hypotension). The administration of dibenzyline (20 μgm./100 gm.) or chlorpromazine (2.5 mgm./100 gm.) completely reversed the lethal tendency, a 100 per cent recovery now being obtained. Both of these agents appeared equally effective, and no significant differences between these two sets of rats were observed.

DISCUSSION

The present experiments have provided new information concerning several aspects of the shock syndrome. First, the data indicate that the gastrointestinal tract and the liver represent the major areas where decompensatory pooling develops following protracted hemorrhagic hypotension. Secondly, a new drug, chlorpromazine, was found to be effective in counteracting the lethal effects of severe hemorrhage, especially in eviscerated rats. Thirdly, the protective action of dibenzyline was shown to be associated with the effect of this agent on some aspect of liver function. Finally, the beneficial action of chlorpromazine and dibenzyline could not be ascribed to their ameliorative effect on either tolerance to blood withdrawal or the curtailment of decompensatory uptake of blood.

Surgical removal of the intestinal viscera and isolation of the liver from the circulation served to attenuate the phenomenon of "uptake" from the blood reservoir. This decompensatory phase of the shock syndrome has been ascribed to congestion and pooling of blood in the intestinal tract by Frank and Selkurt and their associates and in the liver by Friedman, and Shorr and their associates. Fine and co-workers have suggested that a bacterial toxic factor may represent the precipitating episode directly responsible for the intestinal congestion during shock. The present investigation demonstrates that both the intestinal tract and the liver contribute to the pooling or uptake phenomenon during the latter stages of hemorrhagic shock in the rat. Removal of the gut alone had a proportionately greater influence on the resultant uptake of blood than did the presence of the liver alone. Following extirpation of both the gut and the liver, significant pooling failed to develop during hemorrhagic hypotension in any of the remaining vascular beds, skin, lungs, skeletal muscle, or kidney. Circulatory collapse in eviscerated rats does not appear to be peripheral vascular in origin, but rather the result of failure of a central regulatory mechanism.

Chlorpromazine completely reversed the lethal outcome of hemorrhagic shock in all three categories of experimental animals. This agent represents a comparatively new development in the field of blocking drugs and as pointed out by Laborit has been used extensively in hibernation anesthesia. Little information has been provided concerning the precise pharmacologic potentialities of chlorpromazine with reference to circulation. Only preliminary reports have appeared dealing with the uses of chlorpromazine in low concentrations to attenuate the vascular collapse during severe hemorrhagic shock or trauma.

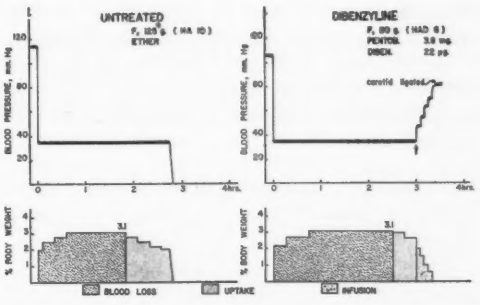

Fig. 3. Both chlorpromazine and dibenzyline increase capacity to withstand hemorrhagic hypotension in partially eviscerated animal (H.A. preparations). These rats live longer at 35 millimeters of mercury than do completely eviscerated animals at 40 millimeters of mercury. With dibenzyline (20 μgm./100 gm.) rat HAD 6 recovered, in contrast to lethal outcome in untreated counterpart (HA 10).

Experiments in this laboratory (14) indicate that chlorpromazine in the anesthetized rat serves as an adrenergic blocking agent, and frequently reverses the pressor response to intravenous l-arterenol or epinephrine. No other form of autonomic blockade was demonstrated. It is presumed that chlorpromazine may also act centrally in hemorrhagic shock, chiefly because of its demonstrated effect on centrally mediated reflexes, its depressant and anesthetic potentiating properties, and its striking improvement of respiration during shock.

Dibenzyline also has been reported by Wiggers and Baez and co-workers to attenuate the decompensatory sequelae of hemorrhage in the dog and rat. It is significant that in the present studies the drug showed no protective action in the absence of the liver, actually predisposing to collapse in these rats. A further difference between dibenzyline and

chlorpromazine is seen in their effect on the uptake of blood in control animals subjected to hemorrhage. Rats treated with dibenzyline survive an otherwise lethal procedure, despite an even greater uptake of blood than in untreated controls. Chlorpromazine, on the other hand, blunted considerably the uptake phenomenon in control rats treated in a comparable manner. The mechanism of action of dibenzyline with reference to the liver remains obscure, although it has been suggested by Mazur and associates that the drug acts to prevent the reduction of SH groupings in vasoactive substances such as ferritin.

It might be anticipated that the protection afforded by dibenzyline or chlorpromazine would be accompanied by an improved capacity to tolerate blood loss, or by a reduced tendency for uptake during shock. This was not found to be the case in both eviscerated and partially eviscerated (H.A. preparations) animals. Almost identical patterns of blood loss and uptake of blood were exhibited in both treated and untreated rats, with no apparent relationship to the ultimate recovery of the animal.

It should be emphasized that the present experiments deal with acute survival following a "lethal" stress procedure. Unfortunately, no long term survival observations were possible with this type of experimental preparation. Protection with both chlorpromazine and dibenzyline has been demonstrated, however, in reference to long term survival following exposure to Noble-Collip drum shock and graded hemorrhage in normal rats (15).

SUMMARY

1. Removal of the gastrointestinal tract and liver in anesthetized rats minimized the decompensatory uptake of blood following prolonged hemorrhagic hypotension.

2. The uniformly lethal outcome of exposure to a hypotension of 35 to 40 millimeters for 3 hours, in controls, in eviscerated and in H.A. preparations, could be counteracted by pretreatment with chlorpromazine.

3. Dibenzyline exerted a protective influence on the lethal course of hemorrhagic hypotension only when the liver was present.

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THE VASCULAR RELATIONS OF THE PANCREAS

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THE close relationship between surgery and anatomy is never more clearly expressed than in the development of new surgical procedures. The surgical attack on the pancreas will be considered less hazardous in proportion as the blood supply of this organ and its other important vascular relations are better understood. The blood vessels around the pancreas are large, important, and more numerous than the current brief textbook accounts indicate. There are 8 major arteries of the pancreas, rather than the 3 commonly described in textbooks. The 8 major arteries of the pancreas are: (1–2) anterior superior and posterior superior pancreaticoduodenal arteries, (3–4) anterior inferior and posterior inferior pancreaticoduodenal arteries, (5) dorsal pancreatic artery, (6) inferior pancreatic artery, (7) pancreatica magna artery, and (8) caudal pancreatic arteries. The general disposition of these vessels is shown in Figures 1 and 2.

The arteries of the pancreas lie predominately on the posterior surface of the pancreas. This is in keeping with the vascular pattern of most of the abdominal viscera. Originating from a dorsally placed aorta the vessels maintain a similar relation to each organ. In the case of the pancreas, only the anterior arcade, and that merely in part, lies on its anterior surface. The other vessels lie on its posterior surface.

OPERATIVE EXPOSURE

The anterior surface of the pancreas is readily approached by opening the greater omentum along the greater curvature of the stomach (Fig. 3). When the stomach has been elevated from the anterior surface of the pancreas and reflected upward toward the diaphragm, the large gastroduodenal artery is found to lie immediately behind the first part of the duodenum, its right gastroepiploic branch being mobilized with the stomach and its anterior superior pancreaticoduodenal branch lying upon the surface of the head of the pancreas partly buried beneath areolar tissue (Fig. 1). The gastroduodenal artery, with its contribution to the anterior pancreatic arcade, is the only vessel readily apparent when approaching the pancreas anteriorly. When ligating this vessel to obliterate its entire contribution to the pancreatic circulation, the ligature must be placed within 1½ centimeters from its origin from the hepatic artery, because the important posterior superior pancreaticoduodenal artery branches from the gastroduodenal within that distance from the hepatic at the medial aspect of the upper part of the head of the pancreas (Fig. 2). The other important arteries to the pancreas lie against its dorsal surface and cannot be isolated except by further mobilization of the pancreas. For this reason it would seem reasonable that during any procedure requiring partial or total pancreatectomy the gland should be completely mobilized first, giving the operator ready access to its dorsal surface before attacking the body of the gland proper.

The dorsal surface of the pancreas is approached by an incision through the peritoneum along the right margin of the second part of the duodenum (Fig. 3). This is the established exposure for access to the retropancreatic portion of the common bile duct. For greater exposure the hepatic flexure of the colon can be detached from the right posterior abdominal wall and retracted medially from the anterior surface of the second part of the duodenum. The operator's hand is then passed behind the duodenum and head of the pancreas, mobilizing these organs medially and upward. The entire dorsal surface of the pancreas rests in an avascular fusion fascia, a plane of areolar tissue which was formed embryologically by the fusion of two layers of peritoneum. The plane separates readily by blunt dissection. When the pancreas is mo-

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bilized from the posterior abdominal wall through this avascular fusion fascia the gland is separated from the inferior vena cava and aorta posteriorly and the portal vein, splenic vessels, and superior mesenteric vessels are carried with the gland anteriorly and upward as far as the attachment of the superior mesenteric vessels to the vena cava and aorta.

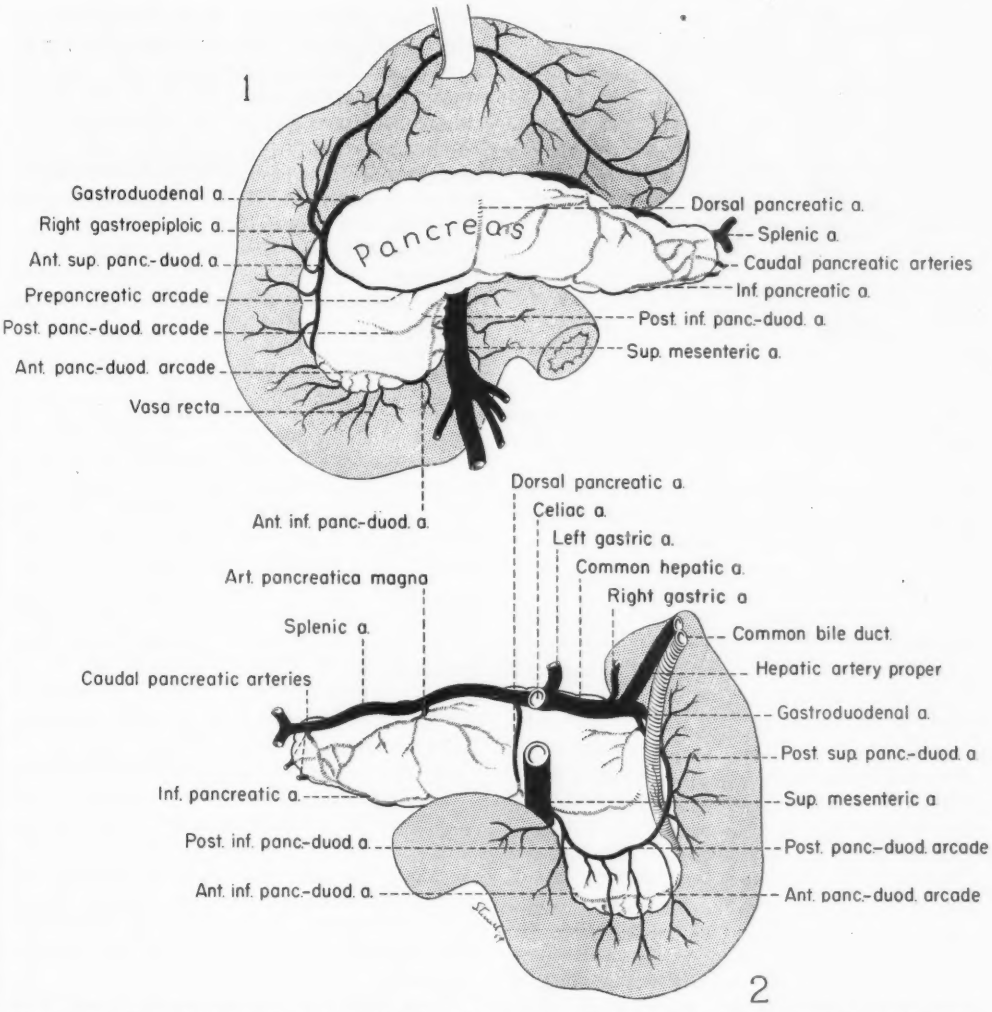
The portal vein and the splenic and mesenteric vessels are usually closely applied to the dorsal surface of the pancreas, lying in grooves in the pancreatic substance and well overlaid by connective tissue (Fig. 2). The superior mesenteric vessels below lie within the clasp of the uncinate process and the neck of the pancreas. The splenic vessels are frequently extremely tortuous, the artery appearing coil-like on the superior dorsal surface of the pancreas, some of the coils projecting above the superior margin of the gland.

Partial pancreatectomy with resection of the body and tail is made easier by concurrent splenectomy. Ligation of the splenic artery close to the celiac axis and of the adjacent dorsal pancreatic artery dorsosuperior to the neck of the gland allows a vertical section of the neck of the gland and its mobilization to the left without serious hemorrhage. As it comes into view a ligature may be placed on the splenic vein to the left of its junction with the inferior mesenteric vein. With occlusion of these major vessels little bleeding should be encountered from the numerous small superior pancreatic vessels, the pancreatica magna, or the caudal pancreatic vessels.

THE ARTERIAL ARCADES

The head of the pancreas rests in a meshwork of vessels, with an arterial arcade on both anterior and posterior surfaces (Figs. 1 and 2). These arcades, or "double arterial arches," received early descriptions from Winslow (1732), Haller (1742, 1764), and Wiart (1899). They were called "peripancreatic arterial circles" by Testut (1893). The anterior arcade is formed by the union of the anterior superior and anterior inferior pancreaticoduodenal arteries (Figs. 1, 2). The superior artery arises (100 per cent in 150 specimens) (14) as the termination of the gastroduodenal artery as the latter vessel divides on the anterior surface of the head of the pancreas. The inferior artery arises from the superior mesenteric artery separately or in union with the posterior inferior artery (62 per cent), but frequently takes origin from an upper jejunal branch either separately or in common (36.6 per cent). Pictorial analysis of these and other variations in this vessel is made in Figure 4. One must always bear in mind when attempting to isolate and ligate the inferior pancreaticoduodenal arteries that they arise as a single trunk in only 68 per cent of cases; in 32 per cent of cases there are separate origins for the anterior and posterior vessels. There is also double hazard when the inferior pancreaticoduodenal vessels arise (36.6 per cent) from the smaller caliber jejunal vessels, instead of from the large superior mesenteric artery. In such cases the pancreatic vessels pass behind the superior mesenteric artery, and as an added danger the jejunal vessel may be mistaken for them and suffer ligation, with possible embarrassment of circulation in the proximal jejunum. The shorter more cephalic posterior arcade is completed by the important posterior superior pancreaticoduodenal artery (retroduodenal artery of Edwards and Michels). This vessel, the first branch of the gastroduodenal artery (Fig. 2), sinks deeply between pancreas and duodenum adjacent to the right upper border of the gland to reach the posterior surfaces of these structures. Its close relation to the common bile duct is to be noted.

One must clearly grasp the concept of the two arterial arcades, one on either surface of the head of the pancreas (Figs. 1 and 2), before attempting any operation in this region. Without its full appreciation massive bleeding may be encountered through blindly cutting across one of these two large arterial systems. The arcades act as shunts between the hepatic and superior mesenteric arteries and bleeding from them can sometimes be as brisk as cutting either of the two larger vessels. When one dissects a large number of cadavers one is impressed by the fact that the arcades are of vastly different calibers (14), some small and difficult to find, while in other specimens they are of such large caliber that they lie like ropes over the surface of the gland and may be comparable in size to the gastroduodenal artery.



Figs. 1 and 2. Respectively anterior and posterior views of the pancreas showing the principal arteries and arterial arcades.

The arcades provide vasa recta to the anterior and posterior surfaces of the duodenum and to both surfaces of the pancreas. It is also significant that the superior end of the arcades do not "quite reach" the first 4 centimeters of the duodenum, so that this part of the duodenum receives its blood supply from a group of rather small vessels from several sources.

In the early embryo the vasculature of the gastrointestinal system is a meshwork of vessels and channels, first formed in the blood islands of the yolk sac. As specific vessels develop to serve the various gastrointestinal parts more adequately, other less essential channels disappear and only the distant ends of the larger channels remain as a meshwork of smaller vessels. In a general way, this explains why there are variations among the pancreatic vessels in different individuals; and why they are of varying calibers. The pancre-

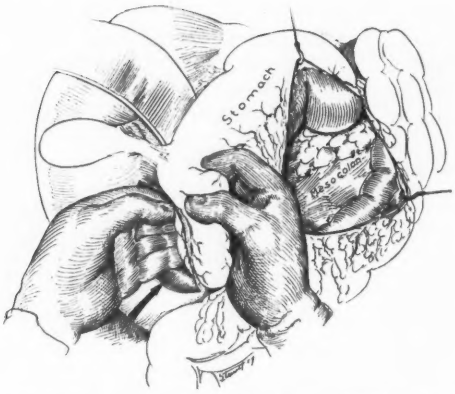


Fig. 3. Operative exposure showing mobilization of the duodenum and the head of the pancreas.

atic circulation appears to be formed at a zone of junction or overlap of the vascular beds of the celiac and mesenteric vessels.

THE SHUNT AND OTHER VARIANTS

Occasionally there is a separate large direct arterial shunt across the anterior face of the head of the pancreas (Fig. 5). When this channel is present it is frequently as large as the gastroduodenal artery itself. In our series it occurred in nearly 5 per cent of cases (7 of 150) either as a separate and distinct vessel (Fig. 5) or as a gross enlargement of either the anterior or prepancreatic arcade (Fig. 1).

Another variation relating to the anterior surface of the pancreas is the presence here of the middle colic artery. Normally a high branch of the superior mesenteric artery directed into the mesocolon at its attachment over the pancreas, the middle colic artery or an accessory middle colic artery took origin from pancreatic vessels in 7.4 per cent of our cases. These vessels appeared as terminal branches of the gastroduodenal as it divided into the right gastroepiploic and anterior superior pancreaticoduodenal arteries or as branches of dorsal pancreatic artery as it emerged and divided under the neck of the pancreas.

THE RELATION OF THE POSTERIOR ARCADE TO THE COMMON BILE DUCT

There is a close relationship between the posterior superior pancreaticoduodenal artery and the common bile duct, recognition of which is important to those attempting mobilization of the retropancreatic portion of the duct. This artery originates from the gastroduodenal artery about 1½ centimeters from the latter's origin from the hepatic artery. In about 80 per cent of cases it passes anterior to the duct, and then, almost constantly, winds about the duct posteriorly as shown in Figure 2, giving off tiny end arteries to this portion of the duct. This relationship has been noted by many observers, especially do Rio-Branco and Petrén.

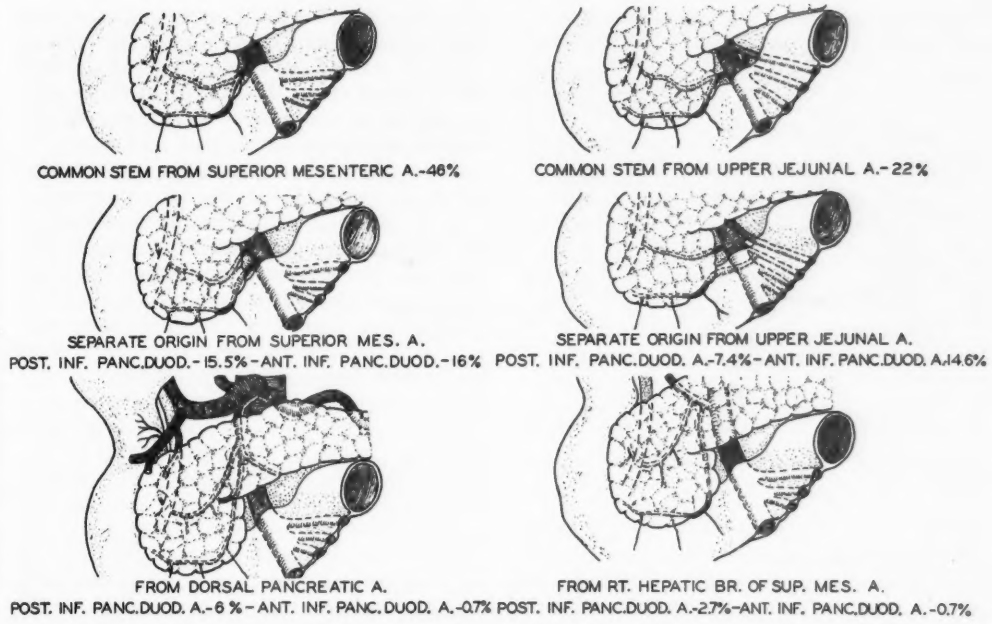
THE DORSAL PANCREATIC ARTERY

This is a vessel of some size, described by Haller as early as 1742 under the name of great superior pancreatic artery. It must be respected as a frequent "fourth" branch of the celiac axis. By definition it may arise directly from the celiac axis, or within 1.5 to 2 centimeters from the axis from either the hepatic or splenic arteries. It varies greatly in size, being as small as the cystic artery, or as great as one-third to one-half the caliber of the hepatic artery itself. It occurred in 90 per cent of our 150 dissections (14). Arising posterior to the gland, it descends to the inferior border of the neck where it divides (Figs. 1 and 2). A right branch curves onto the head of the pancreas, supplying the uncinate process and contributing to a small prepancreatic arcade (Fig. 1). The left branch of the dorsal pancreatic artery is usually that vessel recognized as the inferior pancreatic artery and described in the following. The dorsal pancreatic artery is occasionally a high branch of the superior mesenteric.

From a surgical standpoint the dorsal pancreatic artery is especially vulnerable because of its origin at the superior posterior aspect of the gland. It is not readily available except by approaching the pancreas posteriorly or above. Operators who have inadvertently transected this hidden vessel may have thought that they had penetrated the larger mesenteric artery or the portal vein.

THE INFERIOR PANCREATIC ARTERY

The inferior pancreatic artery occurred in 100 per cent of our dissections, as a vessel


COMMON STEM FROM SUPERIOR MESENTERIC A.-46%
COMMON STEM FROM UPPER JEJUNAL A.-22%
SEPARATE ORIGIN FROM SUPERIOR MES. A.
POST. INF. PANC.DUOD.-15.5%-ANT. INF. PANC.DUOD.-16%
SEPARATE ORIGIN FROM UPPER JEJUNAL A.
POST. INF. PANC.DUOD. A.-7.4%-ANT. INF. PANC.DUOD. A.14.6%
FROM DORSAL PANCREATIC A.
POST. INF. PANC.DUOD. A.-6 %-ANT. INF. PANC. DUOD. A.-0.7%
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POST. INF. PANC.DUOD. A.-2.7%-ANT. INF. PANC.DUOD. A.-0.7%

Fig. 4. Varieties of inferior pancreaticoduodenal arteries. The anterior inferior pancreaticoduodenal artery has a 100 per cent occurrence, the posterior inferior pancreaticoduodenal artery, a 99.3 per cent occurrence. (From original of Fig. 3 in R. T. Woodburne and L. L. Olsen, *Anat. Rec.*, 1951, 111: 265.)

which runs along the inferior border of the body of the pancreas, frequently embedded in the dorsal aspect of that border (Figs. 1 and 2). It usually arises as the left branch of the dorsal pancreatic artery (84 per cent), or exists as a continuation of the left branch of the anterior superior pancreaticoduodenal artery (10 per cent). Occasionally (1.3 per cent) the inferior panerratic artery may arise separately from the superior mesenteric artery.

THE PANCREATICA MAGNA ARTERY

This vessel occurred in 64.7 per cent of our dissections, and uniformly ran its course on the dorsal surface or embedded in the gland (Figs. 1 and 2). It is a large pancreatic branch of the splenic artery entering the pancreas at approximately the junction of its middle and distal thirds. A vessel in this position and frequently oriented along the duct system was described in this manner by Quain over a century ago.

THE CAUDAL PANCREATIC ARTERIES

Caudal pancreatic vessels (Figs. 1 and 2) to the tail of the pancreas were found in 78.7 per cent of our dissected specimens. They may be represented by a single channel or several vessels arising from the distal end of the splenic artery, from the left gastroepiploic artery, or from one of the terminals of the splenic artery at the hilum of the gland.

THE VEINS OF THE PANCREAS

It may be said that the veins of the pancreas are only second in importance to the arteries and require the surgeon's attention earlier since they are generally superficial. As the greater omentum is mobilized it will be observed that the right gastroepiploic vein passes from the gastrocolic ligament into the right extremity of the transverse mesocolon and, lying in the mesocolic attachment across the head of the pancreas, reaches the superior mesenteric vein into which it empties. The right gastroepiploic vein receives the anterior

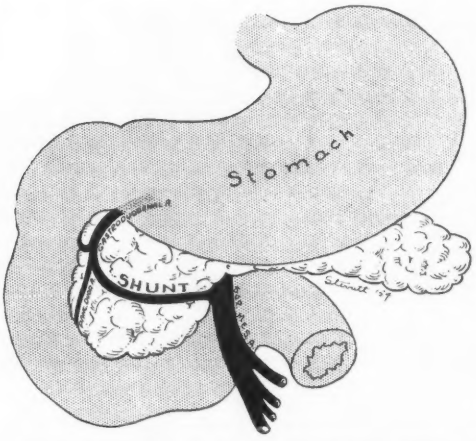

Fig. 5. A type of shunt that occasionally exists across the anterior face of the pancreas.

superior pancreaticoduodenal vein as it makes contact with the head of the pancreas. One or more colic veins from the hepatic flexure and transverse colon so frequently empty into the right gastroepiploic that it was designated the gastrocolic vein by Descomps and de Lalaubie in 1912.

The veins of the head of the pancreas have been well described by Petrén and by Falconer and Griffiths. In addition to the anterior superior pancreaticoduodenal vein mentioned the anterior venous arcade provides an anterior inferior pancreaticoduodenal vein which, like the artery, passes to the dorsum of the uncinate process and behind the superior mesenteric vessels to terminate most commonly in the uppermost jejunal vein. This termination is frequently by a common trunk with the posterior inferior pancreaticoduodenal vein. Occasionally the superior mesenteric vein is the site of termination. The posterior venous arcade provides a posterior inferior pancreaticoduodenal vein terminating in much the same manner as the anterior inferior vein and also a posterior superior pancreaticoduodenal vein which is tributary to the portal vein in almost all cases.

The posterior venous arcade shows the same close and spiral relation to the common bile duct as has been mentioned for the artery. Petrén makes mention of a vein lying horizontally across the head of the pancreas in an intermediate position in 50 per cent of cases which he named the anterior medial pancreaticoduodenal vein. We have identified it occasionally in our specimens. It empties into the superior mesenteric vein.

The veins of the neck, body, and tail show somewhat less constancy though a pancreatica magna vein and caudal pancreatic veins may be expected regularly with the corresponding arteries. An inferior pancreatic vein runs medialward along the dorsoinferior border of the pancreas emptying in about equal numbers into the superior mesenteric and inferior mesenteric veins and less frequently into the splenic vein. A complete dorsal pancreatic vein corresponding to the artery of the same name occurs only occasionally. The inferior pancreatic vein substitutes for it in part, at other times it is characteristic of the neck region of the pancreas and, turning under it, terminates in the splenic vein. An occasional vein draining the right portion of the neck into the superior mesenteric vein just before it disappears under the neck of the gland was designated by Kirk the pancreatic cervical vein. Numerous pancreatic veins also emerge from the dorsal aspect of the gland and empty directly into the splenic vein.

The pattern of formation of the portal vein behind the neck of the pancreas is, of course, well known. It should be recognized that the splenic vein lies inferior to the artery, frequently close to the inferior border of the pancreas. The inferior mesenteric vein arches retroperitoneally above the duodenojejunal flexure to terminate in the splenic vein (60 per cent) and the superior mesenteric vein (40 per cent). The coronary vein descends diagonally across the celiac axis or its hepatic or splenic branches behind the pancreas to terminate for the most part in the portal vein near its commencement though quite frequently into the terminal portion of the splenic vein. The termination of the posterior superior pancreaticoduodenal vein in the portal vein has been mentioned.

SUMMARY

1. There is a general pattern in the network of arteries about the pancreas, which is formed

from 8 major vessels. Each of the major vessels is discussed with emphasis upon their surgical implications.

2. There are arterial arcades on both the anterior and posterior surfaces of the head of the pancreas. These arcades vary greatly in caliber, some small and some very large. The arcades represent arterial shunts between the hepatic and superior mesenteric arteries.

3. There are usually 2 superior and 2 inferior pancreaticoduodenal arteries.

4. The inferior pancreaticoduodenal vessels may arise from the first jejunal artery rather than from the superior mesenteric.

5. The posterior superior pancreaticoduodenal artery has a close spiral relation to the common bile duct.

6. Emphasis is placed on the fact that most of the major vessels of the pancreas course on the dorsal aspect and are not readily accessible anteriorly. This is especially true of the large dorsal pancreatic artery which may arise as a fourth branch of the celiac axis.

7. A surgical exposure of the posterior surface of the pancreas is described and the posterior plane of avascular embryonic fusion fascia emphasized.

8. There is an occasional arterial shunt directly across the anterior surface of the head of the pancreas between the gastroduodenal and superior mesenteric arteries. It may be of large caliber, frequently almost as large as the gastroduodenal artery.

9. The arteries of the pancreas are accompanied by veins, generally of the same name, which are located more superficially. A brief discussion of the veins of the pancreas has been given together with the relations of the great veins adjacent to the gland.

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CHILBLAINS

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CHILBLAINS, perniosis, the pernio syndrome, dermatitis hiemalis, erythrocyanosis, erythrocyanosis frigida, erythrocyanosis crurum puellarum, erythrocyanose sur malléolaire, nodular vasculitis, erythema induratum, and Bazin's disease are terms which have been applied to various stages in the progress of a single disease entity. There is no reason to retain more than the simplest of the many terms attached to the condition, and since the term chilblain means "a blotching or ulceration of the skin resulting from (damp) cold," that would seem to be the one to retain. The common factors in all of the clinical manifestations represented by the synonyms mentioned are susceptibility and chronic exposure to low grade cold and damp. For this reason chilblains, as we propose to call the condition, are exceedingly common in the British Isles and the report of McGovern and Wright suggests a rising incidence in America.

In its early stages there is a distinct seasonal incidence, the symptoms developing with cold weather and disappearing with warm weather. In its later stages when chronic ulceration of the skin is present the lesions tend to persist all year round. Thus chilblains may be divided into two stages: an acute stage which is completely reversible and a chronic stage in which permanent tissue changes have developed and in which ulceration may or may not be present—a stage which is never completely reversible. Chronic chilblains have aroused the greatest controversy and in this report it is proposed to discuss chiefly our experience with 26 such patients in whom sympathectomy was performed.

ACUTE CHILBLAINS

Acute chilblains are a common complaint during the winter months in this country and more than three-quarters of the patients seen are under the age of 20 years with the highest incidence in the adolescent female. The toes, feet, and legs, inadequately and sometimes only partially protected by sheer stockings, short skirts, and flimsy footwear, are predominantly affected in the female while the hands are more frequently involved in boys.

With the onset of cold weather the extremities begin to burn and itch and, if examined at this stage, the skin will be red or cyanotic, cold, and slightly swollen. Blebs of varying size, sometimes hemorrhagic, with well defined margins develop if the exposure is prolonged. Upon coming into a warm environment the itching and burning become intensified and too rapid warming by placing the extremities near an open fire or in hot water may produce vesicles not previously apparent. The acute stage is fully developed within 12 to 24 hours of the initial exposure and lasts only a few days if the exposure to cold is not repeated. If hemorrhagic blisters have developed these usually rupture with the development of a superficial, weeping, raw-ham tinted patch. This fades to a brownish hue which persists covered by a thin layer of scaly skin (Fig. 1). A similar delay in healing occurs if the blisters become infected or the skin broken or burned by exposure to heat or to vigorous massage during the recovery period.

The mechanism of acute chilblains is severe spasm of the blood vessels to the skin upon exposure to cold and damp in a susceptible individual. Since not everyone develops chilblains an individual susceptibility, as yet of unknown nature, must be proposed. Skin biopsy in the acute stage reveals a nonspecific inflammatory reaction with transudation of serum and perivascular infiltration of the small blood vessels in the papillary layer of the cutis. A certain immunity seems to develop as the patient grows older, but in some individuals a recurrence develops with middle age, and chronic chilblains are then established, the initial trouble in adolescence being forgotten.

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In the acute stage avoidance of further exposure of the limbs and the body to chronic chilling and the provision of a warm environment and adequate clothing and shoes will ensure no further attacks. If blisters are present they should not be pricked but should be kept dry and exposed unless weeping is troublesome, when dry dressings may be applied. Systemic antibiotics should be exhibited if secondary infection becomes imposed; excessive heat, vigorous massage, and local applications are avoided. If the precautions against cold are rigidly followed no further attacks should develop, but if they do, the onset of warm weather leads to a spontaneous cure.

Fig. 1. Healing stage of acute chilblains of the toes.

CHRONIC CHILBLAINS

If exposure to cold is repeated and prolonged, irreversible changes develop in the exposed parts and the condition progresses over several winters, or rarely within a single season to a stage of permanent discoloration, nodule formation, and finally ulceration of the skin. It is this chronic stage of chilblains which has led to most controversy and to repeated attempts to separate the stages of the downhill course to irreversibility into separate clinical entities. Thus, if cyanosis predominates the condition has been termed erythrocyanosis, erythrocyanosis frigida, or erythrocyanosis crurum puellarum; if nodule formation predominates, nodular vasculitis or erythema induration; and if ulceration predominates, ulcerative erythema induration or Bazin's disease. The common factor in chilblains is exposure to and sensitivity to prolonged low grade cold, the clinical picture varying with the duration of exposure, the individual susceptibility of the tissues and the stage at which the patient seeks advice.

It is generally agreed that, to produce chilblains, chronic cooling of the extremities re-

Fig. 2. Early stage of chronic chilblains in a 30 year old woman with a 12 year history. Note the thick ankles, prominent hair follicles, and pigmentation.

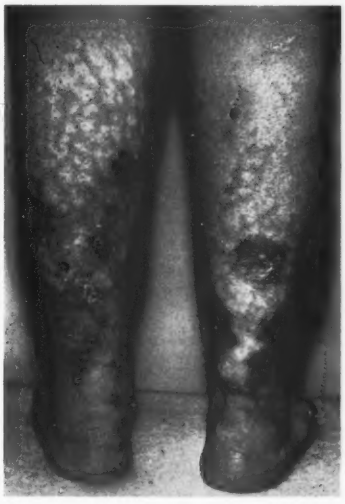
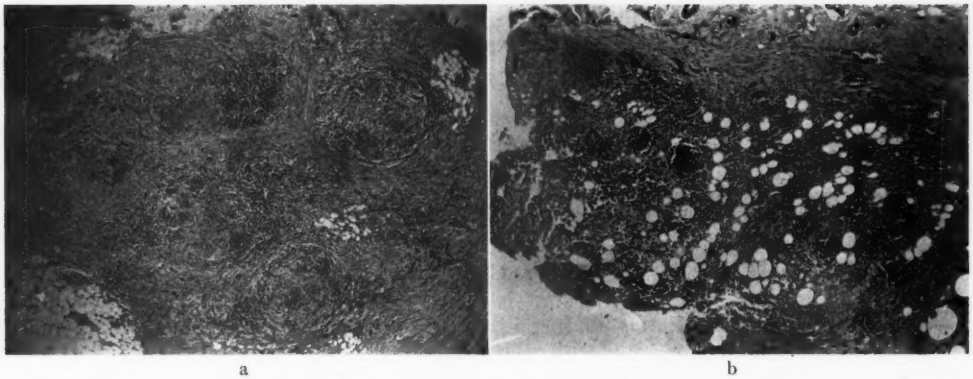


Fig. 3. Advanced stage of chronic chilblains in a 24 year old woman with a 10 year history of chilblains. Picture taken after 1 week of bed rest and bradasol dressings.



a b

Fig. 4. a, Shows numerous "tubercle-like" nodules with central caseation, giant cells, epitheliod cells, and lymphocytes. Biopsy is from the patient whose legs are shown in Figure 3. Culture and guinea pig inoculation from the other half of this biopsy were negative. Hematoxylin and eosin, ×40. b, Section from ulcer of leg of a 60 year old woman showing caseation, giant cells, and epitheliod cells in tubercle arrangement. Hematoxylin and eosin, ×40.

quires in addition some as yet obscure background of vascular susceptibility in the tissues of the limbs. Seldom can the nature of this defect be ascertained but there is no doubt that anterior poliomyelitis renders a limb unduly susceptible to the effects of cold. Five of the patients in this series had suffered from poliomyelitis as children. Excessive fat in the legs is a predisposing factor probably because fat is a poorly vascularized tissue. Most, though not all, patients seen with this condition have stout legs and thick ankles. Bellocq has shown that the vascularity of the skin in the lower parts of the legs is poorer than that elsewhere in the limb so that the development of chronic chilblains is doubtless the result of a combination of factors. Tuberculosis has been suggested as a causative factor when ulceration is present. In common with other authors none of the material biopsied in this series has yielded a positive culture directly or a positive guinea pig inoculation; only 3 patients had a history of tuberculosis and none of these had an active lesion. When chronic chilblains develop in a patient suffering from tuberculosis or other general disease it is more likely that the chronic chilblains are the effect of reduced general health and resistance rather than that they are a strictly tuberculous lesion.

Clinical features. All too often in eliciting the history of a patient with chronic chilblains, exposure to damp cold is overlooked or, if noted, is not considered relevant to the condition with which the patient presents. All 26 patients considered in this report were females. Their ages varied from 16 to 60 years with an average of 35 years; 17 of the 26 females were under the average age. A history of acute chilblains in the past or in association with the present condition was invariable. A seasonal incidence, there being exacerbation in the winter months and regression in the summer months, was present in all of those who had had poliomyelitis and in 17 of the remaining 21 patients. Three complained of erythralgia in the warm weather.

The lower one-third of both legs is symmetrically involved unless the chronic chilblains develop in a paralyzed limb when the condition is restricted to that limb. In the young woman it is often a disease of fashion and no weightier indictment of the chief precipitating factor can be found than that of Lewis: "It came in with short skirts and thin stockings and will go out with them." This opinion is supported by the rarity of the condition in men, whose legs are well protected. In the older woman, and those with chronic poliomyelitis, the legs are usually excessively fat and the ankles thick. In both age groups the condition is reported to be more common when resistance is lowered by some general disease, most frequently heart disease, and in the poorer classes, probably as an expression

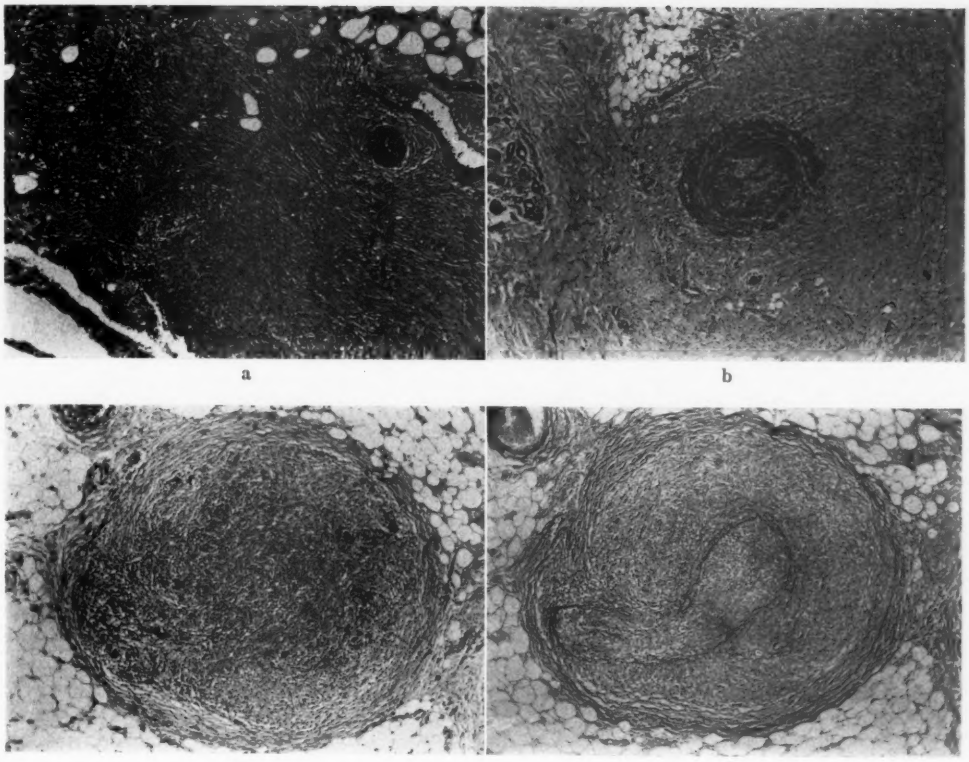
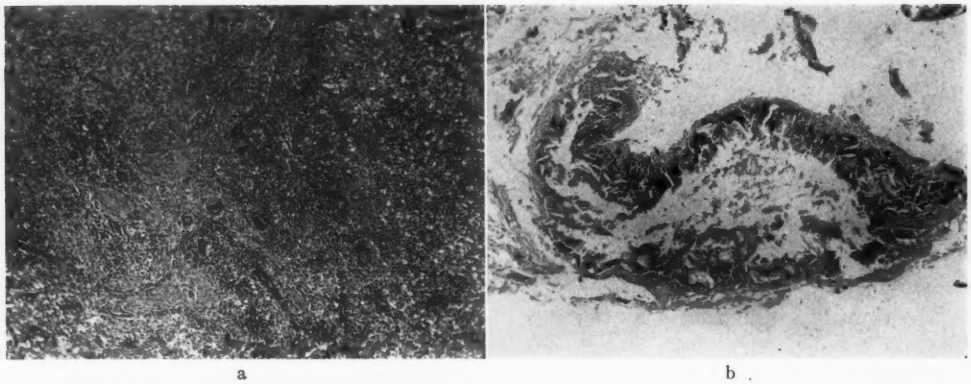


Fig. 5. a, Biopsy section from an ulcer of the leg of a 19 year old girl showing an active granulomatous reaction with nonspecific mononuclear cells, epitheliod cells, and an advanced degree of obliterating endarteritis. Hematoxylin and eosin, ×40. b, Another field from the biopsy shown in Figure 4b with a completely obliterated artery embedded in fibrous tissue. Hematoxylin and eosin, ×40. c, Hematoxylin and eosin, ×40. d, Elastic preparation of, c, showing a small artery the seat of a "pseudotubercle." Biopsy from the patient shown in Figures 3 and 4a.

of their environment and poorer nutrition. These associations have not been prominent in the cases here considered.

Persistent, blotchy discoloration of the lower third of both legs develops in cold weather. Occasionally the legs may be affected up to the knees and the inner aspects of the thighs, and rarely the arms may be similarly involved in the triceps brachii region. The blotches are dusky and reddish purple, fading into the surrounding skin which is abnormally cold and redder than normal, with prominent hair follicles (Figs. 2 and 3). At first the condition is more disfiguring than troublesome and with the advent of warm weather rapid recovery occurs. After several winters or rapidly during one season the discolored patches become larger, swollen, resistant, and nodular. The nodules are elevated above the level of the skin to which they are attached. Firm, painful, and tender to touch they vary in size from a few millimeters to several centimeters in diameter. At first the nodules regress or even disappear in warm weather but eventually persist all year round and ulcerate.

Actual breakdown of a nodule is usually preceded by a period of itching and the development of a small, painful violaceous blister. This ruptures with relief of pain to leave a shallow ulcer which heals to leave a permanently pigmented scar over which the skin is atrophic, covered with fine scales, and prone



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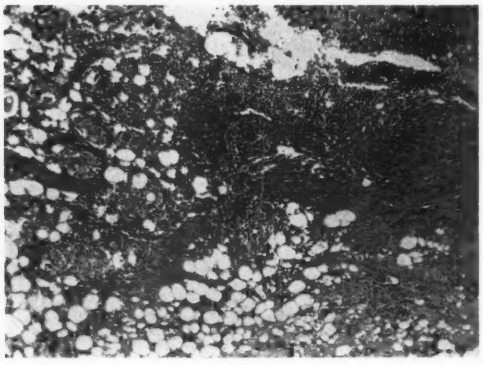

c

Fig. 6. a, b, and c. Three sections from 2 patients suffering from fat necrosis of the breast. If it were not for the presence of recognizable breast tissue in other fields of these sections they would be indistinguishable from chronic chilblains. Compare particularly with Figures 4b and 5a. Hematoxylin and eosin, ×40.

to recurrent ulceration. At first the ulcers heal in warm weather, but if treatment is not undertaken they become larger, coalesce, and remain open all summer (Fig. 3). The legs become permanently swollen and the inguinal lymph nodes are usually enlarged.

Almost half of the patients with chronic chilblains are said to have acrocyanosis but only 4 of our 26 patients were so affected. All the major arteries are palpable in the affected limbs and the veins are clinically normal. Arteriography has been carried out in 10 patients and has revealed no abnormality in the arteries. Blood chemistry and serology have been uniformly noncontributory, and no patient has been hypertensive. In 3 patients there was a family history of chronic chilblains; in only 1 patient of 7 tested was the Mantoux intradermal test significantly positive.

Pathology. The histologic picture in chronic chilblains is characterized by its nonspecificity which is not surprising since the skin and subcutaneous tissues, including the blood vessels, have a limited range of response to noxious agents, including cold. The mechanism underlying the tissue changes is at first recurrent anoxemia which progresses to chronic ischemia if the stimulus is sustained. At this stage the circulation no longer recovers completely between attacks and organic tissue damage develops to be followed by attempts at repair.

The dominating feature in any one section depends upon the chronicity of the lesion, the presence or absence of ulceration, and the degree of superimposed inflammation. The first change is saponification of fat which leads to the presence of numerous giant cells of the foreign body type, and surrounding the area of fat necrosis are lymphocytes, fibroblasts, and granulation tissue (Fig. 4a and b). The activity and degree of the inflammatory response are largely proportional to the extent and duration of the ulceration. The picture is completed by a variable degree of obliterating endarteritis and in some cases the vessels themselves are the seat of "pseudotubercles" (Fig. 5a, b, c, and d). The vascular reaction usually consists of intimal proliferation, medial hypertrophy, and perivascular inflamma

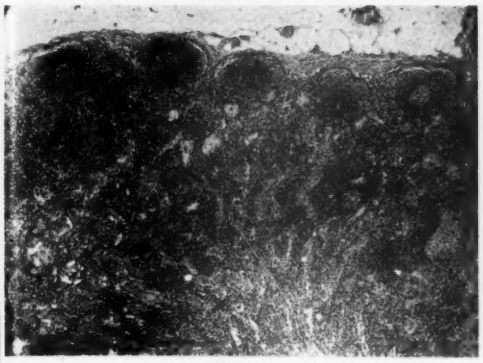

Fig. 7.

Fig. 7. Lymph node from the groin of the patient shown in Figure 3 and whose biopsy sections are shown in Figures 4a and 5c and d. Hematoxylin and eosin, ×20.

Fig. 8. The same patient as shown in Figure 3, two years after bilateral lumbar sympathectomy. Pigmentation persists and scaly, atrophic skin covers the sites of previous ulceration.

Fig. 8.

tion. With very little alteration this picture would fit that of fat necrosis of the breast or systemic nodular panniculitis (Fig. 6a, b, and c). If several sections are taken from the same limb variations in the basic pattern described will be seen. Fat necrosis may predominate in one, extensive fibrosis of the subcutaneous fat in another, and endarteritis in still another. Biopsy of the inguinal lymph nodes has never shown more than sinus hyperplasia and fibrosis compatible with nonspecific inflammation in their drainage territory (Fig. 7). The failure to detect tubercle bacilli by examination or by culture in our material accords with the experience of McGovern and Wright and Telford. Bazin's clinical descriptions would fit chronic chilblains as we understand them and since he included no histology in his study the basis for incriminating tuberculosis in this condition is founded on most tenuous grounds and should, along with attempts to dissect a single disease into several clinical entities, be dropped.

Treatment. There is no specific treatment for chronic chilblains except suitable prophylaxis in an individual who has shown an abnormal response to the effects of damp cold. A warm environment, warm clothing, and wet-proof footwear are essential and, for those who can afford it, temporary or permanent residence in a warm, dry climate may be advised.

In severe cases with painful ulceration bed rest with elevation of the limbs will relieve the symptoms. Excessive warmth will often cause exacerbation of pain. Local application of 1/1000 bradasol[1] is soothing, nonirritating and, being oily, prevents the dressings or bed clothes from adhering to the ulcers. In several cases a full course of streptomycin and isonicotinic acid hydrazide was given with no improvement of the ulceration. Cultures are made of material from the surface of the ulcers, and if complicating secondary infection is present the appropriate antibiotic is given systemically. The ulcers are biopsied for histologic examination, culture, and guinea pig inoculation. A regional lymph node is similarly treated.

Since an essential factor in the first instance is chronic arteriolar vasospasm, sympathetic denervation of the involved limbs would seem to be logical. This procedure has been carried out in 40 limbs (26 patients) with good results and no recurrence of ulceration although the longest follow-up is only 6 years (Fig. 8). The subjective improvement is more marked than the objective appearance of the legs would suggest. The sense of coldness, heaviness, and

[1]Bradasol is domiphen bromide.

burning is relieved, as is the ulceration, but the thickness of the ankles, the pigmentation, and the color changes are not substantially improved. This is probably not surprising since the more important factor in the mechanism of chilblains is the local vascular fault. In several cases added comfort and improvement have followed the wearing of one-way stretch elastic stockings. Generally speaking, lumbar sympathectomy is a worth-while procedure particularly if performed before ulceration has developed.

SUMMARY

"Chilblains," meaning a blotching or ulceration of the skin resulting from cold, has been found a more acceptable term than others to describe the acute and chronic effects of damp cold upon the extremities. Acute chilblains predominantly affect the feet, hands, and legs of adolescent females whereas chronic chilblains with discoloration, nodule formation, and ulceration of the legs are chiefly a disease of women in the third and fourth decades of life. No evidence has been found to support a tuberculous origin for the disease. Avoidance of cold, sensible clothing, and, in chronic cases, lumbar sympathectomy are the essentials of treatment.

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MANAGEMENT OF MALIGNANT DISEASE IN THE NEIGHBORHOOD OF THE HIP

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THE treatment of malignant disease in the neighborhood of the hip is obviously dependent on a number of factors among which are: the age and general condition of the patient, the nature of the lesion, its relationship to adjacent vital structures, its tendency to early or late metastasis, and its sensitivity to roentgen therapy.

Of the primary malignant bone tumors only two, Ewing's sarcoma and reticulum cell sarcoma (Fig. 1), are sufficiently radiosensitive to warrant the employment of roentgen therapy as a matter of choice.

If surgical treatment is indicated it may involve resection (Fig. 2a and b) or such radical measures as amputation at the hip joint or hindquarter. In each case the decision must be made anew; and while the findings of the roentgenologist and the pathologist are essential, in the final analysis the responsibility for the decision rests with the surgeon alone.

With the steady improvement in operative mortality rates and the realization that these patients may be able to wear prostheses successfully, hemipelvectomy has unquestionably increased in popularity while hip joint disarticulation is less often employed. Without wishing to appear reactionary, it is our belief that there is still an important place for hip disarticulation and we deprecate the tendency to select hemipelvectomy for cases hitherto adequately treated by hip disarticulation. Such practice in our opinion results in unnecessary morbidity and in increased mortality (1).

Broadly speaking, hindquarter amputation (interilioabdominal amputation or hemipelvectomy) may be indicated in cases of malignant disease of the pelvis and upper thigh which, in the absence of distant metastasis, cannot be better treated by nonsurgical measures and in which the disease cannot be successfully removed by hip disarticulation, local excision, or other less radical measures (Fig. 2c).

The indications for hemipelvectomy may be outlined as follows:

Bone tumors—
- Benign
  1. Extensive giant cell tumor, recurrent, otherwise inoperable, after failure of conservative surgery and/or irradiation
  2. Extensive osteochondroma unsuitable for resection with evidence of transition to secondary chondrosarcoma
- Malignant
  1. Secondary chondrosarcoma of innominate bone or of proximal end of femur too extensive for hip disarticulation
  2. Selected cases of low grade osteogenic sarcoma in same locations
  3. Malignant giant cell tumor

Soft part tumors—
- Beyond the scope of less radical procedures
  1. Liposarcoma
  2. Myosarcoma
  3. Fascial sarcoma
  4. Melanoma
- Alveolar soft part sarcoma
- Synovial sarcoma

Infections—
- Rare instances of tuberculosis involving innominate bone, unsuitable for any other treatment
- Rare instances of other infectious processes under same conditions

Hindquarter amputation is an excellent example of a procedure which was soundly conceived, practiced on a small scale with exceedingly high operative mortality, and largely abandoned only to be revived under much better operating conditions, anesthesia, and postoperative management (5). Gordon-Taylor (6, 7) has contributed enormously to this revival. His series of cases is the largest ever

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Fig. 1. Reticulum cell sarcoma of left ilium in a 44 year old man. Treatment with x-rays and Coley's toxins.

collected from a single institution. In the United States there are several sizable collections, notably, that of Grantley Taylor (10) in Boston, and Pack (8, 9) and his co-workers in New York. The latter comprises 48 cases of which 41 were performed at Memorial Hospital. Our own experience is based on a series of 30 cases all but 1 of which were treated at Memorial Hospital; thus the total experience at that institution covers 70 hemipelvectomies.

Of our series of 30 hemipelvectomies, 27 were performed for bone sarcoma and 3 for soft part sarcoma; or more specifically, 20 for chondrosarcoma arising on a pre-existing chondroma or osteochondroma, 6 for osteogenic sarcoma, and 1 for malignant giant cell tumor. The 3 soft part sarcomas are excluded from further consideration in this report.

The youngest patient in our series was 17 years old, and the oldest 65, the average age being 40.8 years. We have not as yet encountered a child whom we thought should be subjected to hemipelvectomy. There were 22 males and 5 females.

Site of tumor. The tumor was located in the ilium in 18 cases, pubis in 4, ischium in 1, and the proximal portion of the femur in 4 cases. In 2 of the iliac cases, recurrent disease had followed hip disarticulation for a primary lesion in the proximal femur, suggesting that both of these patients should have had a hemipelvectomy in the first place.

Treatment prior to admission. When first admitted for hemipelvectomy the majority of patients had been subjected to various procedures, such as, biopsy, roentgen therapy, and, in 14, incomplete attempts at removal of the tumor had been carried out. The complications attendant on this prior therapy included: wound infection, recurrence in the overlying soft parts, and alteration in the histologic grading. Furthermore, previous roentgen therapy had made the subsequent hemipelvectomy more difficult, the complications more frequent, and in some instances, it had undoubtedly affected the ultimate outcome adversely. Therefore, in the face of a possible hemipelvectomy we strongly urge that preoperative irradiation be avoided. Of the 27 cases under consideration only 8 patients had received no treatment prior to our observation.

Diagnosis. As in bone sarcoma in general (1), the diagnosis rests upon a careful appraisal of all symptoms and signs with special emphasis placed upon a history of pain, swelling, and disability. Physical examination may be singularly unrewarding or it may reveal a massive swelling, depending on the nature of the lesion. One should not lose sight of the fact that the innominate bone and the proximal portion of the femur are so extensively covered by soft parts as to enable a bone sarcoma to reach considerable size before the swelling becomes apparent on inspection or even by palpation.

Roentgen findings. The value of adequate roentgenographic examination can scarcely be overemphasized. Films should be taken both for bone and soft part detail, and stereoscopic views may be of great assistance. Such examination gives a reliable conception of the size and extent of the lesion, as well as the degree of involvement beyond the midline or of encroachment upon the sacrum or pubic symphysis. Moreover the roentgenographic features revealed will often permit the roentgenologist to predict the type of tumor present. Chest films are, of course, essential, for the finding of pulmonary metastasis would seem to preclude further consideration of the operation. In no instance in this series was there any evidence of lung metastasis at the time of operation.

Histologic diagnosis. Before seriously considering hemipelvectomy a microscopic examination of biopsy material is essential. Wheth-

a b c

d e

f

Fig. 2. a, Bulky growth of lesion arising from left ilium of a 28 year old man with hereditary chondrodysplasia. Biopsy report was chondroma. b, Wide local resection of left iliac wing and tumor arising therefrom. Microscopic sections reported benign chondroma. Note other areas of chondrodysplasia in upper ends of right and left femurs. c, Two years later there was local recurrence and aspiration biopsy suggested malignant tumor. No evidence of pulmonary metastasis. Other lesions of multiple chondrodysplasia showed no significant change. d, Gross specimen removed by hemipelvectomy. Microscopic examination reported chondrosarcoma. e, Postoperative roentgenogram showing complete removal of the left innominate bone and lower extremity. Again note other lesions of chondrodysplasia in right ilium and femur. f, Patient wearing prosthesis and able to walk well without crutch or cane 6 months after hemipelvectomy.

er this material is obtained by open (surgical) biopsy or by aspiration is a matter of choice and depends upon the conditions that obtain in the hospital where the operation is to be undertaken. We warn, however, that in tumors of cartilage origin the biopsy report of chondroma does not necessarily mean that the tumor is not a chondrosarcoma as microscopic examination of the entire specimen may prove it to be. We have learned that a large cartilage tumor of the innominate bone or the proximal end of the femur, which is causing pain and which on the x-ray films appears to be malignant, should not be considered benign even though the biopsy report is chondroma. Moreover, it should be emphasized that a histologic diagnosis of chondroma on previous operation or biopsy is no assurance that the tumor may not at a later date prove to be chondrosarcoma (Fig. 2d). In short, the clinical and roentgenographic findings are more valuable than is the microscopic report when sarcoma is suggested by the former and chondroma by the latter.

Clinical considerations. There are several practical considerations in connection with the operation of hindquarter amputation which may be mentioned. In our series of 27 operations for bone tumors the only death occurred in a patient who had been given hexamethonium hypotensive anesthesia. We believe that the entire operation was otherwise uneventful and that had this patient not received this combination of drugs, the mortality rate in our series would have been nil.

Our practice is to disarticulate at the sacroiliac joint and at the symphysis pubis (Fig. 2e); anything short of this is not, in our opinion, a true hindquarter amputation. We do not ligate the common iliac artery but rather the external iliac. By placing a temporary occlusion clamp (seraphin) on the internal iliac artery we prevent blood loss and yet preserve some of the blood supply to the posterior flap that otherwise would be destroyed were the common iliac ligated. In a previous paper we have described in some detail the operative technique and the complications, and since our impressions in the interim have not materially altered we will not repeat them here. Suffice it to say, prolonged drainage and delay in accomplishing complete wound healing are still our most troublesome sequelae.

We have not, as yet, felt disposed to advise the operation for purely palliative purposes and thus have never attempted it when evidence of lung metastasis was present. We have also believed that where life expectancy of only a few months (1 to 3) was present its advisability was questionable. Thus we have preferred other palliative measures, such as cordotomy, in these instances and have been less inclined to continue to advocate the operation for osteogenic sarcoma. Yet experience with one or two patients from whom hemipelvectomy has been withheld and who continued to suffer with their primary tumor should be sufficient to convince any member of the medical profession that the operation may have a definite place even when carried out as a purely palliative measure. We cannot express this conviction more clearly than to quote from Gordon-Taylor (7), as follows: "What the shorter survival figures fail to show is the relief from pain which the procedure usually affords. The contribution to the patient's happiness and well being is considerable, even though death from pulmonary metastases may occur a few months later."

Progressive improvement in the manufacture of prostheses for patients requiring hemipelvectomy or hip disarticulation has done much to render these operations more acceptable. Prostheses can now be made that are functionally useful and quite well tolerated by the patient (Fig. 2f). Eleven of our hemipelvectomy patients have worn limbs successfully.

RESULTS

In the first 21 consecutive hemipelvectomies for bone tumors there was no operative fatality; the twenty-second patient died of the effects of the operation; in other words, there was 1 death in 27 cases or an operative mortality rate of 3.7 per cent. In the 27 cases the 2 indeterminate cases consisted of 1 postoperative death and 1 death from causes other than the disease. In the 25 determinate cases there were 12 failures—10 dead from bone cancer and 2 alive with bone cancer—and 13 successes (52 per cent)—all alive and free from evidence of bone cancer.

More important, no doubt, is the result of the operation based on a 5 year follow-up, as follows: Of the 7 patients operated upon 5 or more years ago 1 died 3 years after operation without evidence of bone cancer (indeterminate case). Of the 6 determinate cases, 4 patients are dead and 2 are alive and free of evidence of bone cancer, i.e., a 5 year survival rate of 33⅓ per cent.

A study of the end results in relation to the *type* of bone sarcoma found reveals the following: Of the 25 determinate cases 12 patients with chondrosarcoma, 2 with osteogenic sarcoma, and 1 with malignant giant cell are alive; 6 patients with chondrosarcoma and 4 with osteogenic sarcoma are dead. In other words, of the 18 patients with chondrosarcoma, 12 (66 per cent) are alive, and of the 6 with osteogenic sarcoma, 4 (66 per cent) are dead.

We have long believed that the ideal indication for hemipelvectomy was the so-called secondary chondrosarcoma of the innominate bone or proximal portion of the femur; in

other words, in chondrosarcoma arising on a pre-existing central chondroma or osteochondroma the outlook for this tumor, regardless of the site of origin, is very much better than it is for osteogenic sarcoma. This view is substantiated by a study made of 52 secondary chondrosarcomas in which we found the 5 year survival rate to be 51.7 per cent (3).

Hip disarticulation. Hip disarticulation is another measure for dealing with selected cases of cancer in the neighborhood of the hip joint. It was performed 52 times on our service at Memorial Hospital between 1932 and April 1, 1954. In 41 instances the lesion was in bone and in 11 cases it was of soft part origin. Of the 41 patients with bone tumors 27 are dead, 9 are alive less than 5 years, and 5 for more than 5 years (or 15 per cent of the determinate cases). In the 11 patients with soft part tumors, 6 are dead, 4 are alive less than 5 years, and only 1 for more than 5 years (or 15 per cent).

Of the entire series of 52 cases of hip disarticulation, only 1 patient was later subjected to hemipelvectomy because of stump recurrence. Of the remainder there was evidence of local recurrence in 5 cases indicating that in the rest of the cases death was due to distant metastases.

Nonsurgical methods of treatment. We prefer roentgen therapy to radical surgery for the radiosensitive primary sarcomas known as Ewing's sarcoma (endothelioma) and reticulum cell sarcoma. Ewing's sarcoma has such a uniformly fatal prognosis regardless of the method of treatment employed, and roentgen therapy can usually control the primary tumor, that we have virtually abandoned radical surgery for this disease (4). Reticulum cell sarcoma also seems to be capable of long term control in approximately half of the cases by means of roentgen therapy together with the administration of Coley's toxins so that amputation has not seemed justified as a standard method of attack. As to dosage, we use tumor doses in the range of 4,000 roentgens for Ewing's sarcoma and 3,600 roentgens for reticulum cell sarcoma.

Plasma cell myeloma is another type of malignant disease obviously unsuitable for radical surgery, and this is especially true in cases in which bony destruction may appear in the region of the hip. Here we use roentgen therapy for the principal symptom-producing areas only, relying on the oral administration of urethane for its systemic effect. By this combination of therapy, gratifying palliation may be anticipated in a considerable proportion of cases.

Metastatic cancer should be mentioned for completeness especially since numerically it is the most important variety of malignant disease occurring in the bones comprising the hip joint region (2). While the eventual outlook in such cases is obviously unfavorable in a certain number, treatment may relieve pain and prolong life. The measures employed are: supervoltage irradiation, hormone therapy, and neurosurgical measures (cordotomy) for pain relief, radioactive iodine; the surgical procedures include castration and adrenalectomy.

SUMMARY

Malignant disease located in the region of the hip calls for various methods of treatment depending upon its exact location, histologic type, radiosensitivity, and operability.

Hemipelvectomy has a distinct place in the care of patients with malignant disease about the hip. It is especially indicated in low grade, so called secondary chondrosarcoma, where it offers either long term palliation or, in some cases, even a permanent cure.

Hip joint disarticulation also has proved of value in selected cases involving the upper thigh, but in doubtful cases it should be discarded in favor of the more radical procedure since whichever procedure is selected there is little difference in the patient's ability to use a prosthesis.

Roentgen therapy and other agents have been found useful in lieu of surgery for Ewing's sarcoma, reticulum cell sarcoma, plasma cell myeloma, and metastatic cancer in bone.

Before selecting the method of treatment, care should be exercised in the appraisal of each case of malignant disease occurring in the hip area.

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VARICOSE VEIN SURGERY IN THE MANAGEMENT OF THE POSTPHLEBITIC LIMB

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THE treatment of deep chronic venous insufficiency of the extremities when complicated by incompetent superficial varicosities has long been a perplexing medical and surgical problem. This problem has been attacked in many ways by us and others interested in this field. The purpose of the study presented herein is to consolidate 10 years of experience with both the medical and surgical treatment of this problem. It is our belief that the best therapeutic results are obtained when an operative attack is made on the superficial varicosities combined with use of an adequate elastic support.[1] We do not attack the deep venous system directly. The following report concerning 118 extremities operated on at the Mayo Clinic from the middle of 1947 to the early part of 1949 is the basis for this conclusion.

Chronic insufficiency of the deep or internal veins of the lower extremities has long been recognized as a definite clinical entity. This condition is secondary to anything that destroys the normal anatomy of the deep veins and injures their valves or their walls. As Homans has pointed out the commonest cause of such change is thrombophlebitis and the common places of its occurrence are in the calf of the leg and in the iliofemoral region.

Neglected incompetent superficial or saphenous veins alone can produce stasis changes in the leg not unlike those of incompetent deep veins, but in many cases both the superficial and deep systems are incompetent. In such cases we think that adequate surgical treatment of the incompetent superficial varicose veins followed by use of adequate elastic support is the treatment of choice.

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[1]By adequate elastic support is meant the daily use of elastic bandages from the base of the toes to just below the knees with sponge rubber pads over areas of severe stasis. Such support should be applied whenever the patient is on his feet.

INDICATIONS FOR SURGICAL TREATMENT

The main indication for varicose vein surgery in the face of insufficiency of the deep veins is the diagnosis of incompetent superficial veins which are contributing to stasis changes in an extremity by leading directly into an area of stasis change. Significant stasis stigmas include brawny induration, stasis dermatitis, pigmentation, ulceration, or any combination of these four. They may vary from only mild pigmentation and edema to severe brawny induration with ulceration. In each case, the physician must satisfy himself before recommending surgical intervention: (1) that the superficial veins are definitely incompetent and (2) that surgical therapy to these veins would improve the patient's leg. In cases in which a large incompetent superficial vein leads directly into an area of severe induration or ulceration and the patient either will not consistently wear the necessary support or has found that such support failed to prevent progression of stasis changes, surgical therapy is indicated. It should be fully explained to the patient that eradication of his superficial veins will not be a "cure-all" and that use of adequate support on a permanent basis will be necessary.

DIAGNOSIS

The diagnosis of incompetent superficial veins is somewhat more complicated when insufficiency of the deep veins is present also. It is easy to mistake the filling of the superficial vein from below for actual backfilling or incompetency. Likewise, the size of the vein is not always a dependable indication of incompetency, since the superficial veins may be dilated and large from the extra load and yet may not be actually incompetent.

We believe that the examination should be thorough. First a detailed history should be obtained concerning the involved leg. To elicit such a history the patient must be ques-

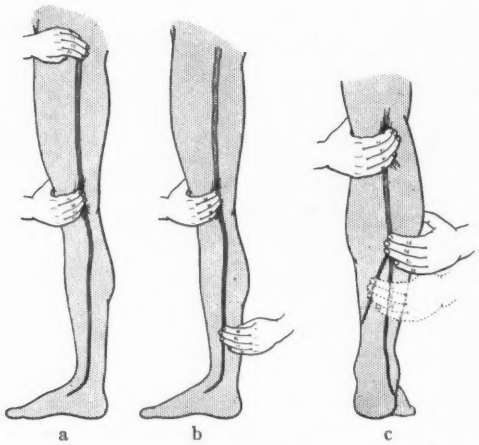


Fig. 1. The Schwartz-Heyerdale test. a, Method of percussion to demonstrate an incompetent greater saphenous vein at the fossa ovalis. b, Method of following course of greater saphenous vein. c, Percussion of an incompetent lesser saphenous vein.

tioned carefully concerning old iliofemoral thrombophlebitis or thrombophlebitis of the calf. Some patients will not give a positive history of phlebitis. For such patients more careful and meticulous questioning about possible injury of the vein associated with previous deliveries, operations, fractures of the lower extremity, and illnesses will be necessary. The majority of patients, however, will recognize that they have had previous trouble in the leg and know the circumstances under which it occurred.

Careful physical examination of the involved leg is the next step in establishing a diagnosis. Areas of stasis change must be located and studied. Edema and cyanosis should be searched for, since they are common signs of deep involvement. The edema is dependent in character but may cause enlargement of the whole lower extremity. The cyanosis is usually found in the lower third of the leg and foot but may be present to the middle of the thigh. Examination next should be directed to the superficial venous system. Often superficial veins will be large, near the skin, and easily visible. In other cases, they will be deep in the fatty subcutaneous tissue and not visible at all. Such veins must then be detected by palpation or compression. We use the compression method[1] (Fig. 1) in every examination for varicose veins for these reasons: (1) It helps in tracing the exact course of the vein. This is accomplished for the greater saphenous vein by compressing the vein at the knee level, by circling the leg with the hand, the finger tips on the vein, and using the other hand (finger tips) to receive the ballottement impact, either above in the thigh and groin or below in the leg. In this manner, it can be determined whether the superficial varices lead into areas with stasis change. (2) The test also serves as a gross measure of the size of the vein. A big impact reveals a large vein, a small one denotes the antithesis or a badly scarred vein.

Although we usually consider the transmission of an impulse in a vein by compression as indicative of incompetency, this test is never used alone, but is followed by thorough tourniquet tests, much like those described by Trendelenburg. Our procedure for this portion of the examination is to have the patient lie on his back on the examining table with his legs raised until all the blood has drained from the superficial veins. He then stands erect and a careful watch is made to detect the rapidity and volume of retrograde or backfilling of venous blood. If it is satisfactorily demonstrated that the filling is retrograde and not from below as is normal, then incompetency has been established. In such a case the blood is again emptied from the superficial veins and a rubber tourniquet is placed at midthigh. The patient again stands. If the greater saphenous vein is incompetent, it will fill down to the tourniquet and remain empty below. When the tourniquet is released, the vein previously empty will fill from above; this gives definite proof that the greater saphenous vein is incompetent (Fig. 2). If the tourniquet at midthigh does not influence the rapid filling of the superficial veins, other diagnoses must be considered. These are secondary dilated superficial veins associated with incompetent deep veins, incompetent lesser saphenous vein, and incompetent per-

[1]By compression, we do not want to infer a percussion movement as described in the Schwartz-Heyerdale test (2). Actually by compression is meant a quick forceful "squeezing of the vein" without releasing it, so that an impact is received above or below when the tested vein is incompetent.

a b c d

Fig. 2. a, Incompetent greater and lesser saphenous veins. b, Veins on the back of the leg do not fill when the greater saphenous vein is held out by a tourniquet and lesser saphenous vein is held out by the thumb. c, The same veins on the back of the leg fill from the greater saphenous vein even though the lesser saphenous vein is held out. d, Filling from incompetent lesser saphenous vein when the greater saphenous vein is held out with a tourniquet.

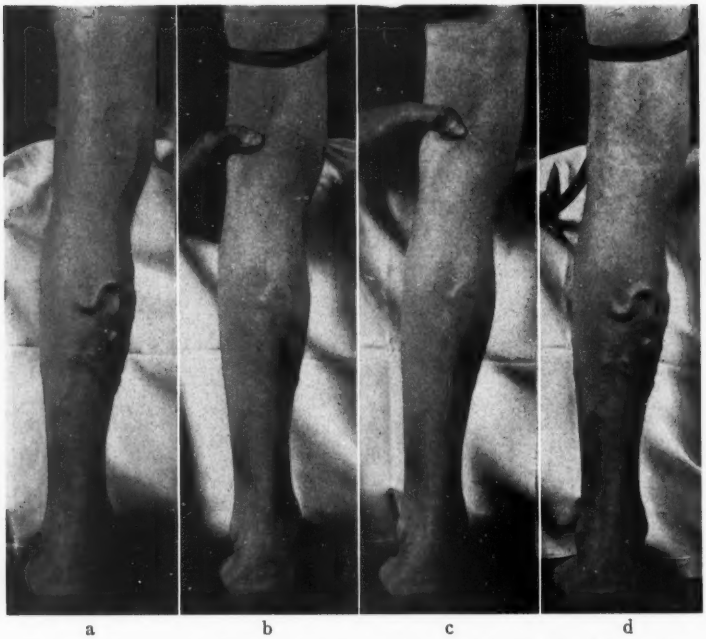
forating veins. The tourniquet method of examination often does not give reliable information about perforating veins. It is more efficient to locate perforating veins by palpating the opening through the fascia where the vein emerges.

We have found that careful examination of each patient for the presence of an incompetent lesser saphenous vein is important.

In making the diagnosis of an incompetent lesser saphenous vein, we use the same group of tests mentioned in diagnosis of the greater sapheni.

The original impression of incompetency of a small saphenous vein gained by compression must always be confirmed by tourniquet tests. This is accomplished by emptying the blood from the superficial veins as previously described and placing a tourniquet around the midthigh to shut out the great saphenous system. Now if the patient stands and the veins in question on the posterior portion of the leg fill, incompetency of the small saphenous is suspected. Further confirmation is achieved, when, with the patient standing while a tourniquet holds out the great saphenous system and the examiner's thumb is held firmly over the popliteal space in the area of termination of the small saphenous, the veins in question do not fill. If these same veins, however, do fill on release of the thumb from the lesser saphenous area, the diagnosis is almost established. To make a final check, the veins are emptied as before, the tourniquet which has been holding out the greater saphenous vein is released while the examiner's thumb holds out the lesser saphenous vein. If the veins suspected of being in the lesser saphenous group do not fill, the diagnosis has been confirmed (Fig. 3).

After the diagnosis of chronic venous insufficiency of the deep veins has been established by history and clinical examination, and after the incompetent superficial veins have been located and traced, there remains only the clinical decision of whether the patient can be benefited by surgical procedures on the superficial veins. Many times, it is



a b c d

Fig. 3. a, Incompetent lesser saphenous vein on posterior surface of leg. b, The same veins on back of leg do not fill when both greater and lesser sapheni are held out. c, There is also no filling when only the lesser saphenous vein is held out. d, There is filling of the veins when only the greater saphenous vein is held out.

hard to determine which set of incompetent veins, deep or superficial, are playing the most important role in causation of stasis. It is our belief that when the superficial veins are incompetent they are definitely a factor in the stasis and it is desirable that they be eradicated by surgical therapy. However, each case is an individual problem and may be handled satisfactorily with adequate elastic support alone, when the risk of operation is great.

PREOPERATIVE PREPARATION

The majority of patients who have chronic venous insufficiency of the deep veins and associated superficial varices have advanced stasis changes which must be treated before surgical treatment can be instituted. If any incision is to be made in or around the area of stasis change, all inflammation, cellulitis, and intense congestion must be eradicated. It is also important that all ulcers be free of infection. We have found that the best treatment is complete rest in bed, except for bathroom privileges, with the involved extremity constantly elevated above the level of the heart. Continuous moist packs of aluminum subacetate (0.25 per cent) or other mild preparations at body temperature are placed over areas of ulceration and stasis change. The wet packs are especially good in areas of stasis where infection or cellulitis has complicated the picture of congestion. This regimen is continued until the ulceration is cleared of infection and a bed of granulation tissue has formed.

In cases in which the ulcer is large, skin grafting is a time-saving procedure. Nevertheless, the actual grafting is always preceded by a sufficient period of elevation and application of wet dressings to the involved leg to clear infection and insure adequate granulation. Multiple pinch grafts or "post-age-stamp" grafts may be used or any split-thickness type of graft. At the time that this

series of patients was treated, skin grafting was accomplished before definitive treatment. At present, however, skin grafting and stripping of the superficial veins are done as one procedure. Adequate elevation, immobilization, and compression of the region of the leg are important points in the postoperative management. Occasionally, an elastoplast "compression boot" is used, especially for those patients who refuse or cannot follow the regimen of rest in bed with elevation of the extremity. Such treatment as a rule gives more erratic results.

SURGICAL PROCEDURES

Following careful shaving and preoperative care of the groin and entire lower extremities with soap and water, alcohol, ether, and an antiseptic solution, we make an incision 5 to 6 inches long (12.7 to 15.2 cm.) just below and parallel to the inguinal crease. The greater saphenous vein and all of its tributaries are widely dissected, severed, and ligated. The greater saphenous vein is traced through the fossa ovalis to its juncture with the common femoral, and doubly ligated flush with this vein, the second tie being a transfixion ligature (Fig. 4). At this point, the common femoral vein is inspected carefully for any residual signs of phlebitis, such as periphlebitic scarring, thickening of the wall, or narrowing of the lumen. If these changes are found, the diagnosis of deep vein injury is confirmed. The fossa is then closed with a purse-string or interrupted suture of plain catgut and if a resection and injection procedure is being done, 2 to 3 cubic centimeters of 5 per cent solution of sodium morrhuate are injected distally into the greater saphenous vein. If stripping is to be done, however, no injection is made at the operating table but accessory incisions are necessary below the knee, on the dorsum of the foot, and over incompetent perforating and tortuous veins which cannot be removed by stripping. A flexible intraluminal stripper then is passed up the greater saphenous vein from the dorsum of the foot to the groin; the vein is secured to the stripper, and then is removed by pulling the stripper upward through both the leg and the thigh (Fig. 5).

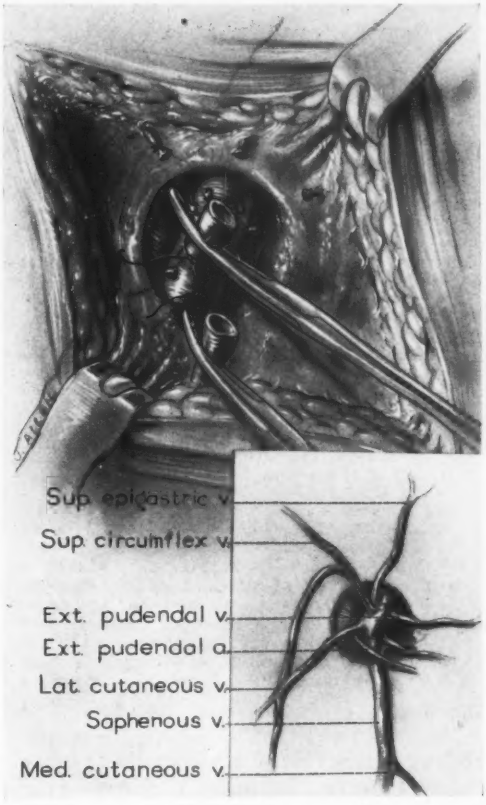


Fig. 4. The technique of division and ligation of the greater saphenous vein flush with its junction with the common femoral vein. *Inset*, Anatomy of the venous tributaries of the greater saphenous vein at the fossa ovalis.

Essentially the same type of operation is done when the lesser saphenous vein is incompetent. In this case, the incision is made ½ to ¾ inch (1.3 to 1.9 cm.) above and parallel to the knee fold. The popliteal fascia is split longitudinally and the lesser saphenous vein is isolated and severed. The proximal stump is then followed to its juncture with the popliteal vein and doubly tied flush with this vein. A dissection of tributaries is carried out much the same as at the groin. The distal segment of the lesser saphenous vein is either injected or stripped much as previously described for the greater saphenous vein, except that the stripper can be passed downward to

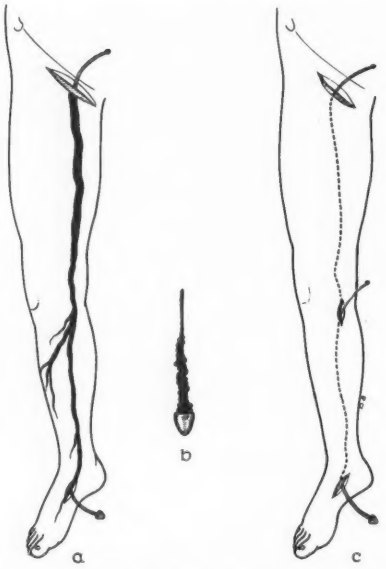


Fig. 5. a, The stripper has been passed from the ankle up the greater saphenous vein to the groin. b, The removed greater saphenous vein telescoped against the head to the stripper. c, Method of passing the stripper the entire length of the greater saphenous vein to the groin or only as far as the knee with later passage from the knee to the groin.

the lateral side of the ankle (Fig. 6). It is our opinion that vein stripping should be very extensive. Our present method is to remove also all incompetent tributaries by direct dissection or undermining with a curved forceps when stripping is impossible. All perforating veins must be ligated individually below the deep fascia of the leg.

POSTOPERATIVE CARE

Following operation, application of pressure dressings to the wounds and adequate elastic support to the involved extremities are provided. For this, we use an elastic type of tape for direct pressure over the wound dressings, then support the entire extremity, foot to groin, by two or three 4 inch elastic wrap-around bandages. If a stripping procedure has been used, additional direct pressure is necessary to help prevent hematoma. This is provided by the placing of abdominal cotton pads over the course of the stripped vein. The patient is put to bed and the legs are kept elevated higher than heart level. If resection and injection have been performed, ambulation is started as soon as the patient recovers from anesthesia. If stripping has been done, ambulation is commenced the following morning. Early ambulation is especially important for patients with deep venous insufficiency. For several weeks the regimen should consist of ambulation alternated with elevation of the legs. This regimen prevents excessive congestion and thus diminishes chances of further thrombotic episodes. Our patients walk for at least 3 to 5 minutes each waking hour of the day and are encouraged to move their legs and body freely while in bed. The average stay in the hospital is 4 to 5 days during which time the wounds are not disturbed. The sutures in the groin are removed on the seventh postoperative day if healing by primary intention has occurred. No sutures are removed from wounds of the thigh, leg, or foot in less than 9 days and if induration of the wound is present this may be postponed until the twelfth postoperative day. On the seventh day following operation, a course of injection therapy is started in order to close any remaining open veins. At the time that this group of patients was operated on many small veins were closed by injection. With the present technique, however, few injections are needed because of the more extensive removal of veins. Solutions used at that time for this purpose include sodium morrhuate in a 5 per cent solution or sodium tetradecyl sulfate (sotradecol) in a 3 per cent solution. Special care must be taken in the injection of veins which are surrounded by areas of severe stasis change because of the danger that the devitalized skin may slough. Pads of sponge rubber are placed over all wounds except the groin on the fourth or fifth postoperative day and are held in position by the elastic bandages. On dismissal, the patient is instructed to wear the elastic bandages to the knee whenever he is on his feet, and this should be done continuously during the first 2 months following surgery. After this period, the patients can adjust the wearing of bandages according to the amount of edema they experience. In cases in which the deep veins have been severely involved, per-

manent adequate elastic support with a sponge pad may be necessary.

Direct pressure and protection, afforded by a sponge rubber pad, have been found to be the best method of preventing recurrent ulceration in extremities having severe stasis changes.

CASES STUDIED

One hundred cases (118 extremities) in which operations were performed for varicose veins at the Mayo Clinic from 1947 to the early part of 1949 form the basis of this report. There was clinical evidence of chronic insufficiency of the deep veins of each limb operated on, and in most cases a history of previous thrombophlebitis of the deep veins was obtained.

OBSERVATIONS

Sex, age, and weight of patient and duration of insufficiency. Our group of patients consisted of 57 women and 43 men. The ages were quite divergent. The ages at time of operation and the approximate lapse of time between the original accident to the deep veins and the operation for varicose veins are given in Table I.

Fifty of the patients were overweight. Twenty of this group were very obese and were operated on, in spite of this, only because of the severity of the stasis changes in their legs. Forty-five patients were in the normal weight range, and 5 were actually underweight.

Cause of deep venous involvement. Most patients included were precise in naming the exact cause and time that they sustained the "milk leg" or phlebitis of the deep veins.

The cause or type of development was indicated as: postpartum phlebitis in 34 extremities, postoperative complication in 26, infections in 13, fracture in 7, trauma in 6, extension from greater saphenous vein to involve femoral vein in 1, and unknown in 31 extremities.

Each of 31 extremities for which no cause was known had definite clinical signs of deep venous involvement, and 9 were found at surgery to have scarring of the femoral vein. It seems likely, therefore, that in a certain number of cases definite injury to the deep veins by thrombophlebitis occurs without recognition.

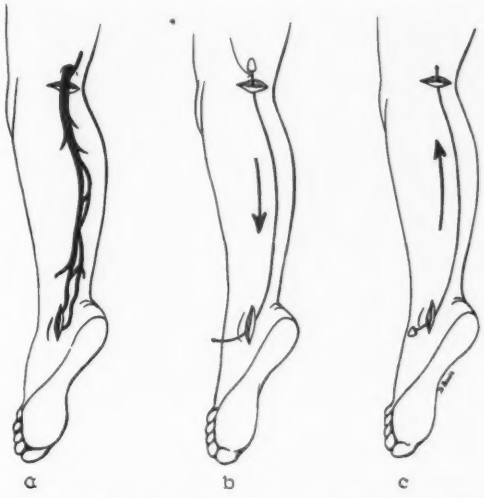


Fig. 6. a, The incompetent lesser saphenous vein and incisions used for stripping. b, The stripper has been passed down the lesser saphenous vein to the lateral aspect of ankle. c, The stripper has been passed up the lesser saphenous vein to the popliteal incision.

Incompetent superficial veins. A detailed analysis of the exact incompetent superficial veins in each extremity operated on will not be presented. In 104 extremities (87 per cent) incompetent greater saphenous veins were operated on, while in 24 extremities (20 per cent) the lesser saphenous veins were operated on. In 14 (12 per cent) the lesser saphenous veins were the only incompetent veins to be treated. These figures concerning the lesser saphenous vein are interesting in light of the fact that our previous studies on cases uncomplicated by deep venous insufficiency demonstrated that only 10 to 13 per cent of our varicose vein surgery dealt with the lesser saphenous vein.

For only 10 of the extremities (8 per cent) was a diagnosis made of incompetent perforating veins, and this diagnosis was proved correct at operation. In all such cases, these incompetent perforating veins were in connection with the greater saphenous system. At present, we are able to locate a much higher percentage of incompetent perforating

TABLE I.—AGE OF PATIENT AND NUMBER OF YEARS BETWEEN INJURY AND OPERATION

Age of patients		Interval before operation	
Age, yrs.	Patients	Years	Patients
20–29	1	0–9	27
30–39	14	10–19	28
40–49	25	20–29	17
50–59	36	30–39	9
60–69	23	40–40	3
70+	1	No record	16
Total	100	Total	100

veins and we attribute this to improved methods of diagnosis.

Symptoms. There was a variety of complaints and symptoms referable to the involved leg. Commonest of these was a "heavy sensation" in the lower extremity or heaviness in the area of stasis change. Eighty-five patients made this complaint. Itching and burning in areas of stasis were commonly associated symptoms of which approximately 60 patients complained. Patients having stasis dermatitis or neurodermatitis frequently complained of itching and burning. Cramping and actual pain in the legs were mentioned by only 50 patients. Usually the cramping occurred in the calf of the leg, and the actual pain was most frequently associated with ulceration.

Stasis changes of the involved extremity included: brawny induration (through cellulitis) in 90 extremities, pigmentation in 67, ulceration in 57, stasis dermatitis in 37, neurodermatitis in 9, subacute cellulitis in 3, and superficial phlebitis in 2 extremities.

In 56 of the 57 legs showing ulceration, an incompetent superficial vein led directly into the area of ulceration. In the single case in which this did not occur, the ulcer did not appear to have any association with the varicosities.

For all but 3 of the 118 extremities there was a history of recurring edema. In only 6 of the extremities were recurrent edema and cyanosis the only findings which indicated that previous injury of the deep veins had taken place.

PREOPERATIVE TREATMENT OF ULCERATION

In 22 extremities it was possible to effect healing of the ulcer before operation. Operations were performed on the superficial veins of 26 extremities when the ulcers were almost healed. All of these ulcers closed while the patients were still under postoperative observation. Six ulcers were of the large type for which skin grafting was required. In each of these instances, multiple pinch grafts followed by adequate compression to the area were used. All of the 6 grafts took satisfactorily. On 3 extremities, the ulcers did not close either before operation or in the early postoperative period. One of these ulcers was suspected not to be of stasis origin however.

SURGICAL PROCEDURES AND FINDINGS

On 62 of the 118 extremities, a resection and injection procedure was done. Most of these procedures were done in 1947 and early 1948. In the remainder of the period under consideration stripping of the veins in part or in whole has been employed in 90 per cent of cases. At first, this consisted of stripping of the greater saphenous vein to the knee with injection of the distal portion. Later, however, extensive stripping from the dorsum of the foot to the saphenofemoral juncture was accomplished in every case possible. Stripping was done on 51 of 118 extremities. On only 5 extremities was resection alone done without either stripping or injection during surgery. On 2 of these 5, resection of the greater saphenous vein at the saphenofemoral juncture was carried out to prevent extension of superficial phlebitis into the femoral vein. In 1 extremity, the thrombophlebitic process had extended into the femoral vein, and the thrombus was removed by suction before the greater saphenous vein was ligated. In the remaining 2 extremities, incompetent perforating veins were resected and the associated saphenous system received no treatment except postoperative injection.

State of canalization of thrombus at operation. In none of the 100 cases was an actual occlusion at the saphenofemoral or saphenopopliteal juncture found at time of operation. Recanalization of the thrombus of the deep veins had occurred in all.

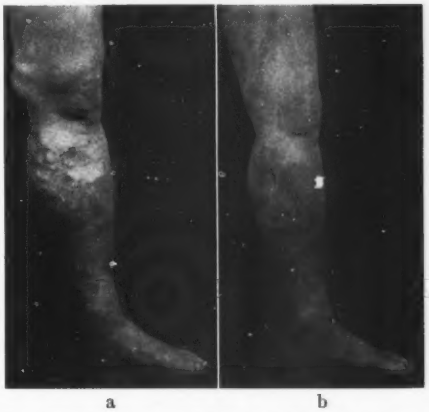
Femoral vein injury proved at surgery. In 40 of the 118 extremities, there was definite evidence of previous injury to the common femoral vein. Criteria used include periphlebitic scarring and, more important, actual thickening of the wall of the femoral vein. In the remaining 78 extremities, there was either insufficient or no evidence that the common femoral vein had been involved by the previous phlebitis. In each of these 78, however, the physical findings were so definite that involvement was suspected to have occurred in another portion of the deep circulation. It was interesting to us to note that in practically all of the 40 extremities with proved involvement of the common femoral vein, the stasis changes were especially severe.

Mortality and morbidity following surgery. There were no hospital deaths in our series. The complications were as follows: deep venous thrombosis, questionable deep thrombosis, flare-up of dermatitis, superficial thrombophlebitis, and considerable edema of the leg—each in 1 extremity; lymphorrhea in 2 extremities; sclerosing accidents (slough) in 3 extremities and failure of operative wounds to heal by primary intention in 7. No new ulcers developed and no pulmonary emboli occurred.

The main complication in the wound, delayed healing, occurred in 5 extremities. The wounds finally healed satisfactorily although it took the wound in the foot of 1 patient 2 months to do so. Suppurative infection was the cause of failure of healing by primary intention in 1 extremity and in another superficial skin slough occurred.

EARLY POSTOPERATIVE RESULTS

Results of operation on the superficial veins were good in 96 extremities. Results were considered good when the wounds healed well, ulcers remained closed, and stasis changes showed definite improvement. In each of these 96 extremities, postoperative edema and swelling were minimal although elastic support was used. Results of operation on 9 extremities were thought to be fair. On 3 of these 9 extremities, open ulcers were present at the time that the patient was dismissed although one of these ulcers was not purely stasis in nature. Four extremities for which the result of operation was fair had persistent dermatitis and induration that failed to improve and 1 each showed persistent edema and severe induration around all the wounds on the leg. Of the 17 extremities in which a combination of wound trouble or some other complication developed after operation, 4 were listed with the group having a fair result because it was believed that, despite the minor complication, the immediate over-all picture was good. In no case was the patient's leg worse after operation than before.



a b

Fig. 7. a, Chronic insufficiency of the deep vein of the leg complicated by a large incompetent greater saphenous vein. b, Same leg after stripping showing diminution of stasis changes and complete absence of greater saphenous vein.

These early good results most certainly were not solely due to the operation. The preoperative and postoperative rest, elevation, and compression were instrumental in reducing stasis in these legs and thus improving dermatitis, induration, and ulceration. The operation, however, did remove what we thought to be a definite factor adding to stasis changes already present, and this was accomplished at no more risk than the same operations on patients having normal deep veins.

FOLLOW-UP STUDY OF 1 TO 3 YEARS

Follow-up data were obtained concerning 104 of this group of 118 extremities in 1950 from 1 to 3 years after operation. Ninety-

a b

Fig. 8. a, Large incompetent lesser saphenous vein associated with chronic insufficiency of the deep vein of the leg. b, Same leg after extensive stripping of lesser saphenous vein showing absence of lesser saphenous vein.

seven of the 104 extremities (93 per cent) were definitely improved and 7 (7 per cent) were not improved. In no case was a patient's leg worse. Forty-three extremities of the improved group were actually seen by us at the clinic and each was greatly improved. Ulcers had remained closed and were more easily kept so, while the stigmas of stasis had disappeared in many instances. Pain in the legs, aching, and heaviness were all subjectively improved, and edema of the involved extremity was more easily controlled by elastic support. No elastic support was being worn on 14 extremities, but in 4 of these, moderate edema of the leg was noted.

Fifty-five patients (61 extremities) who had not returned for examination were contacted by follow-up letters. In this group, 54 extremities were thought by patients to be definitely improved, while 7 had not improved but were not considered worse. Ulceration and the symptoms commonly associated with it were the complaints concerning all of the 7 legs which were not improved. All incisions had healed and in no instance was the ulcer a direct result of the operation. Ulcers on 2 of these 7 extremities had remained open since operation 1 year before; ulcers on 2 had closed after surgery but had reopened; an ulcer was in a new position on 1 extremity, the original ulcer having remained closed; on 1 extremity an ulcer which was grafted had reopened and on 1 a new ulcer which was not present before surgery had developed. On 3 of these 7 extremities with ulceration the patients were not using adequate elastic support while 2 other extremities had been bruised inadvertently since operation with resultant ulceration.

Definite subjective and symptomatic improvement was reported by patients who considered that their legs were improved. Of the 75 traced patients who had pain and heaviness in the leg before operation, only 38 (51 per cent) had this complaint at time of follow-up. Similar reports were obtained from the 52 traced patients who had either itching or burning prior to operation. Only 18 (35 per cent) now complained of itching in the legs, while 12 (23 per cent) still had some burning. No patients in the improved group complained of severe pain or cramps in the leg although most of the 7 patients with ulceration registered this complaint. New symptoms since operation consisted of pain around the site of postoperative injections in 2 cases, tingling in legs in 3, and numbness and coldness in the leg in 1.

Marked change and regression of stasis stigmas have been noted in the legs of those reporting a good result from their varicose vein surgery. Only 32 of the 81 treated extremities in the traced group[1] (40 per cent) showing brawny infiltration still had this change. Eighteen extremities still showed redness of the skin and stasis dermatitis. This was 53 per cent of the 34 traced extremities having this finding before surgery. Pigmentation was the stasis change least affected by operation. It was still present in 54 of the 60 traced extremities (90 per cent) in which it had been present before operation. In many cases, the degree of pigmentation was reported as less, however.

Ulceration has been the most severe stasis finding in this group having chronic insufficiency of the deep veins of the leg. Of the 57 extremities on which ulcers were present when the patient was admitted, 50 (88 per cent)

[1]The term "traced extremities" will be used hereafter to indicate extremities of traced patients which had been treated by operation. Some patients had operations on more than 1 extremity.

have no "open sores" 1 to 3 years after operation. Practically all of this group of patients, however, have worn adequate elastic support since their operation (Fig. 7).

FOLLOW-UP STUDY OF 4 TO 6 YEARS

Follow-up data were obtained concerning 80 of this group of 118 extremities in 1953, from 4 to 6 years after operation. Seventy of the 80 extremities (87 per cent) were definitely improved and 10 (13 per cent) were not improved. In no case was a leg worse.

Eighteen extremities were actually seen by us at the clinic. Sixteen of these were improved and 2 were not improved because of recurrent ulceration. One of the extremities in which ulceration had recurred had been injured recently and ulceration developed despite elastic support and what we interpreted as a good result from the operation. Pain in the legs, aching, and heaviness were subjectively improved in all of these 16 extremities. However, adequate elastic support was being employed in all cases.

Fifty-seven patients (62 extremities) who had not returned for examination replied to follow-up letters. In this group, 54 extremities were considered definitely improved, while 8 were the sites of recurrent ulceration and were believed by patients not to be improved. Ulceration and recurrence of ulceration have consistently been the causative factor in an unsatisfactory result. One ulcer in this group of patients had not healed since operation 5 years before, but all others represented recurrences as the ulcers had healed after superficial vein surgery. Besides the 8 extremities in which ulceration was present at the time of follow-up 6 other extremities listed as improved had been the site of ulceration in the past 3 years but all these ulcers had healed on conservative treatment and had remained healed. On 4 of the 8 extremities with ulceration the patients were not using adequate elastic support.

Subjective and symptomatic improvement was reported by patients who considered that their legs were improved. Of the 65 extremities of traced patients who complained of pain and heaviness in the legs before operation, 36 (55 per cent) still had this complaint.

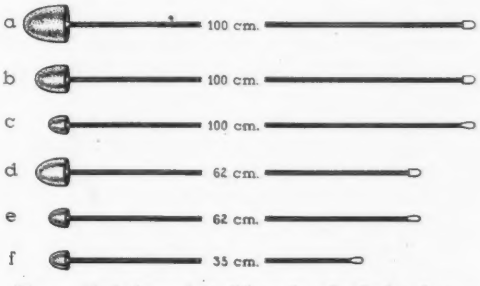


Fig. 9. Variations of the Myers intraluminal stripper.

Similar reports were obtained regarding burning and itching which were experienced preoperatively in 52 of the extremities in the traced group. Now, itching was present in 24 (46 per cent) of these legs and 9 (17 per cent) still had some burning. No patients in the improved group complained of severe pain or cramps in the legs although 5 of the 10 patients with ulceration registered this complaint. No new symptoms since the 1950 follow-up were reported.

Stasis stigmas, likewise, were reported as much improved in the legs of those having good results. Of the 75 traced extremities previously showing brawny infiltration 31 (41 per cent) had this change at the time of this follow-up. Nineteen extremities still showed redness of the skin and stasis dermatitis. This was 66 per cent of the 29 traced patients having this complaint before operation. The 1953 follow-up study revealed again that pigmentation was the stasis change least affected by operation as 32 of the 55 extremities (58 per cent) in the traced group still had it.

We were interested in study regarding ulceration, for now 10 extremities had ulceration as compared to 7 extremities in the 1950 follow-up. This meant that 47 extremities (83 per cent) of the original group having ulceration no longer had it 4 to 6 years after operation for varicose veins. Even though almost all of these 47 patients are wearing adequate elastic support and are adhering to the postoperative regimen which we prescribed, such improvement seems an indication that the operations for varicose veins have been an important adjunct in their treatment. Many of the patients who pre-

viously could not keep their ulcers healed even with support now considered this no problem. Final evaluation will have to come later.

Edema was altered little by operation on the varicose veins. In the 1950 follow-up study, 74 extremities were being adequately supported. This was 71 per cent of the 104 treated extremities in the traced group. In the 1953 follow-up study, 71 extremities (89 per cent) of the 80 extremities traced were being adequately supported. A high percentage of patients stated that edema soon appeared if they went without their support for any period. No patient reported severe, debilitating, or uncontrollable swelling of the involved leg or legs (Fig. 8).

COMMENT

Evaluation of the observations on our 100 patients has made us conclude that definite improvement of stasis changes in the leg can be expected if an incompetent vein leading into such changes is actually eradicated. While this operation in no way alters the deep circulation anatomically, it does nevertheless improve the over-all circulation by removing the superficial of the two sets of incompetent veins. Stasis changes then are corrected more easily or progression is checked especially when the patient fully understands the role of adequate support in the after treatment.

Essentially two types of operative procedures were carried out in our cases. For the first patients a resection and injection type of operation was carried out while for the later patients extensive stripping was carried out. In either case, postoperative injections of small open venous radicles were carried out. We are of the opinion that not only does vein stripping offer a much more complete and thorough procedure, but that the results are better after this operation. At present, all of the operations performed on varicose veins at the Mayo Clinic consist of extensive stripping of the involved veins and ligation of incompetent perforating veins with special attention to the distal third of the leg. A flexible intraluminal vein stripper designed by one of us (T.T.M.) is used for this operation (Fig. 9). Adequate elastic support is recommended to every patient as previously stressed in this article.

SUMMARY AND GENERAL IMPRESSION

A study of 100 patients (118 extremities) having undergone surgical treatment of varicose veins associated with chronic insufficiency of the deep veins of the lower extremities has been reported together with follow-up studies 1 to 3 years and 4 to 6 years after operation. The Schwartz compression method and the tourniquet tests are suggested as diagnostic aids. Careful preoperative and postoperative management, of course, are necessary adjuncts to the carefully planned surgical attack.

The results of surgery in the early postoperative period from 1 to 3 years after operation and later from 4 to 6 years after it were excellent and indicate that surgery on the incompetent superficial venous system is an excellent method of attacking the problem of chronic venous insufficiency of the deep veins of the lower extremities. Continual adequate elastic support is a "must" after these operations. Extensive vein stripping of the incompetent superficial varices is the form of surgical treatment now used at the Mayo Clinic. However, in this particular series resection and injection procedures were employed also to some extent.

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RESECTION OF THE ABDOMINAL AORTA WITH DEFECT REPLACED BY HOMOLOGOUS GRAFT

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CIRCULATION of the blood remained a mystery until William Harvey published "De Motu Cordis" in 1628. Aneurysm, injury, and occlusion of the abdominal aorta had attracted the interest of surgeons long before the time of William Harvey. In our time, we recognize Rudolf Matas, Alexis Carrel, William Stewart Halsted, and others who were intensely interested in this problem. With improvement in surgical technique, anesthesia, antibiotics, the blood and blood vessel bank, we have been able to attack this problem much more vigorously.

The use of wiring, reactive cellophane, and dicetyl phosphate has not proved so successful as we were led to believe formerly. It is now the opinion of most workers in this field that the affected portion of the aorta must be removed to be of maximum aid, be it occluded by thrombus, dilated by aneurysm, or invaded by cancer. The replacement remains a problem although several alternatives are now available.

Vein inlay grafts with and without dicetyl phosphate used in homografts and autographs have not been wholly successful. Vinyon "N" cloth offers much hope in providing a substitute prosthesis which does not deteriorate. The freeze-drying method of preserving grafts is most encouraging, particularly as it appears that homologous grafts will no longer be necessary.

In surgery of the abdominal aorta, most workers have chosen to use homologous arterial grafts. There is still a difference of opinion as to how these grafts should be preserved. When possible, most investigators favor storing in a balanced salt solution with added serum and antibiotics which are considered usable up to 7 weeks, or 42 days. Frozen grafts can be used as an emergency measure when others are not available, but again the consensus is that they are not so satisfactory. Tissue cultures of grafts stored in balanced salt solution have shown most grafts viable after 4 weeks. The graft dies and serves merely as a bridge or scaffold for endothelium and fibrous tissue of the host to grow in and replace the graft. When available, viable tissue should be used by choice to bridge arterial defects in human patients.

In syphilis aneurysm of the aorta occurs almost always in the thoracic aorta and usually with a saccular type defect; in arteriosclerosis it almost always occurs in the abdominal aorta where it is usually fusiform in type, and following trauma.

In the thoracic aorta, resection of an aneurysm offers unique problems in case it is necessary to occlude the aorta completely. Saccular aneurysms may be clamped across the base and excised as shown by Bahnson. The thoracic aorta may be clamped and an aortic homograft inserted as in DeBakey's case (3) and in the one reported by Swan. Lam placed a lucite tube through a graft to conduct blood while the graft was sutured in place.

When it is necessary to resect the arch of the aorta, the problems are multiplied. The heart and lungs are active and function normally, but a shunt must be devised for the head and remainder of the body. This was done by Schafer for 1 patient by using polythene tubing for shunts. He resected a syphilitic aneurysm of the aortic arch by using four shunts, one to each the innominate, the left common carotid, the left subclavian, and the descending aorta. Although the operation was completed, the patient died 1 hour later.

In a large thoracic aneurysm, intercostal arteries coming off the aorta in the region of the aneurysm are usually thrombosed and there is not so great danger from cord damage

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Fig. 1. Case 1. Drawing of aneurysm at time of operation.

as in a normal individual. In Lam's case the aorta was clamped for 25 minutes on one occasion, and again for 15 minutes. In this patient, apparently all the intercostal arteries were divided or had been thrombosed by the aneurysm. The next day there was some evidence of cord damage but recovery was complete. Lam divided all intercostal arteries in 10 dogs; 1 had paralysis of the hind legs, 1 transient paralysis, while 8 showed no evidence of disturbance of spinal cord function. DeBakey (3) clamped the aorta for 45 minutes in excising an aneurysm of the thoracic aorta without causing damage to the cord.

In all operations on aneurysms it is mandatory to remove the sac and not leave it in place after use of a graft. The aneurysmal sac may be the site of an abscess cavity which causes trouble and may lead to death. In case the aneurysm is adherent to a vital structure and cannot be completely removed, the major portion of the sac had best be excised and only a small portion of the wall be left behind.

Aneurysms of the abdominal aorta are almost always arteriosclerotic in etiology, fusiform in type, and arise below the renal arteries. Therefore, the aorta may be clamped for a longer period of time, but removal of the aneurysm is necessitated. Schafer, in his case, cross clamped the aorta for 83 minutes and used a graft 17 centimeters in length including the aortic bifurcation. Schafer comments that it is feasible to resect the entire abdominal aorta with its celiac, superior mesenteric, and renal branches. This, to me, is a large order. DeBakey (4) has resected fusiform aneurysms of the abdominal aorta in 12 instances in which a graft was used to repair the defect. In these cases, the aorta was occluded for 48 to 102 minutes. There was 1 death in the 12 patients.

Although arteriosclerosis is a progressive degenerative disease and removal of one segment of vessel in the form of an aneurysm does not cure the disease, resection of the aneurysm is the procedure of choice. Estes has shown the prognosis of this condition in a study of 102 cases, in which at the end of 3 years over one-half of the patients were dead and at 5 years less than 1 of 5 remained alive. This result is in contrast to the life expectancy of a normal population at this age in which 4 out of 5 will be alive after 5 years. With these factors in mind, we have resected arteriosclerotic abdominal aneurysms in 2 patients.

Case 1. J.W., N. Y. H. 642 211, a 56 year old white male accountant, was admitted to the Muhlenburg Hospital, Plainfield, New Jersey, in September 1951, where examination revealed an aneurysm of the abdominal aorta and a healed peptic ulcer. Following discharge, he remained asymptomatic for a period of 13 months, save for the mass in the left lower abdomen which had been pointed out to him.

Two months before admission, the mass became larger, and the patient developed a dull ache in his right thigh posteriorly. This pain increased until he was admitted to The New York Hospital on November 11, 1952. A diagnosis was made of a fusiform aneurysm of the abdominal aorta due to arterio-

sclerosis, hypertensive cardiovascular disease, and inactive duodenal ulcer. Because of the marked increase in pain, it was thought that the aneurysm was perforating and, therefore, aortograms and additional studies were not undertaken.

Two days after admission, November 13, 1952, a long left perirectus incision was made from the left costal margin down to the symphysis pubis. Upon opening the peritoneum, a large pulsating mass was present which, on dissection, proved to be the entire abdominal aorta starting 1.5 centimeters below the renal arteries and continuing past the bifurcation and into both common iliac arteries. The aneurysm was adherent to the inferior vena cava and in addition appeared on the verge of perforation in places. After careful evaluation and some dissection, it was thought feasible to resect this aneurysm.

First, the aorta below the renal vessels was freed and a clamp placed across the aorta which was thought to give sufficient occlusion to the vessel to control bleeding. As an additional safeguard, the aorta was freed above the stomach and a tape placed around the vessel but not tied. As this was above the renal arteries, it was to be used only in an emergency. When both common iliac arteries were freed, tapes were placed about these vessels. Since now bleeding from the aneurysm was completely controlled dissection was cautiously continued. We were able to free the vein from the aneurysm without fear of tearing the aneurysm and by staying away from the inferior vena cava as much as possible.

After the aorta was occluded by means of the clamp below the renal arteries and with tapes on the common iliacs, the aneurysm was opened and found to contain a large laminated clot. There was very little bleeding. A rather long cuff was left on the proximal aorta, and the remainder of the aneurysm including both common iliac arteries was excised. The mass was large, but there was very little arterial bleeding. The main difficulty rose from small lumbar veins crossing beneath the mass. A human aorta with bifurcation and both common iliac vessels was secured from the New York Blood Vessel Bank (9).

Although the proximal aorta was still flaring and there was some discrepancy in size, an intima-to-intima approximation was done with some difficulty with No. 00000 arterial silk. The needles were small and the aorta contained calcium plaques; however, by placing 4 corner sutures and filling in between, we were able to get a satisfactory suture line. Above the first line a second line was placed, then a third so that a very good anastomosis was effected. The cuff which had been left was tailored and sutured about the anastomosis.

Because of dilatation and marked calcification the common iliac arteries were excised after bilateral ligation of the internal iliac arteries. The common iliac artery of the graft was sutured to the external iliac of the patient by using a continuous mattress everting suture of No. 00000 arterial silk.

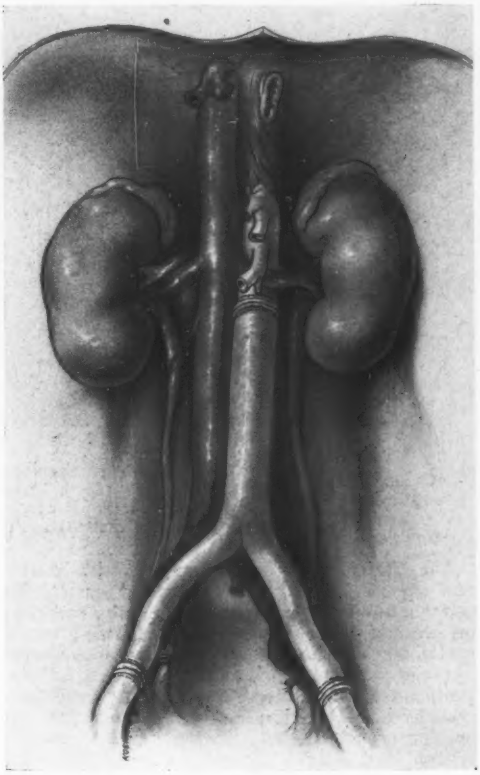

Fig. 2. Case 1. Following resection of aneurysm and replacement of graft. Note both internal iliac arteries are ligated and graft is sutured to external iliacs.

Cautiously releasing the distal clamps first, the proximal next, we found a leak of the proximal aorta posteriorly below the clamp where we had neglected to tie off a vertebral artery. After controlling this, there was very little bleeding from the suture lines. By slow release of clamps, there was very little drop in blood pressure. Since we had removed the inferior mesenteric and ligated both internal iliac arteries, it should be noted that there was no arterial blood supply for the large intestine from the mid-colic artery down, the left colic, sigmoid branches, superior, middle, and inferior hemorrhoidal branches having been deprived of their blood supply. Despite this fact, the colon appeared in good condition. The inferior mesenteric artery had probably been occluded for some time. The abdomen was closed.

Total time of anesthesia was 12 hours and 5 minutes; of operation, 11 hours and 50 minutes. Pressure at start was 120/80; at the end of procedure, 150/100. The clamp was on the aorta for 5 hours and 30 minutes.

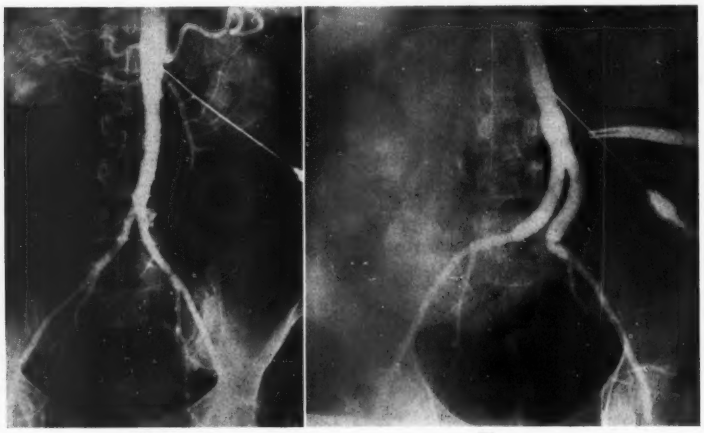

Fig. 3. Fig. 4.

Fig. 3. Case 3. Aortogram showing abdominal aorta displaced to right at the bifurcation. Abdominal mass lay in curve of aorta and on the left side.

Fig. 4. Case 3. Aortogram following resection of tumor and aorta showing graft in position. It can be seen that this graft is a little too long and has buckled.

The patient's immediate postoperative course was smooth, results of observations stable, his peripheral pulses normal, as was the color and temperature of the lower extremities. There was a partial loss of motor sensory function of the lower legs and some fecal incontinence. These findings gradually subsided. A Foley catheter had been placed in the bladder; cystitis followed but was promptly cleared.

Mobilization and ambulation was started on the fifteenth postoperative day. He continued to have moderate diarrhea which had subsided considerably by the time of discharge. Gaining strength rapidly, he was able to walk considerable distances without pain or fatigue on his discharge 35 days after operation.

On December 29, 1952, six weeks after operation, the patient was readmitted because of a rectal stricture. Proctoscopy showed a stricture 10 centimeters from the anal orifice which had a healthy granulating surface, the lumen of the colon being about 1 centimeter in diameter. Biopsy showed only chronic proctitis which was thought to be secondary to operation and loss of blood supply in this region. No surgical procedure was considered necessary and the patient was discharged. Because of a previous reaction following an intravenous pyelogram, we were afraid to do a postoperative aortogram.

At present, 18 months after operation, the patient is working, every day, but there is a dilatation of the thoracic aorta and he is having some cardiac symptoms, having had two episodes of pulmonary edema. Concerning the abdominal complaints, he has been completely cured.

Case 2. Mr. E.A., N. Y. H. 565 382, was first admitted to The New York Hospital on March 15, 1950, as a patient of Dr. William A. Cooper, at which time a diagnosis of chronic duodenal ulcer was made.

Three and one-half years later—November 19, 1953—he was readmitted. His attacks had continued in the meantime, particularly in the summer, and had been getting progressively worse and more frequent. On palpation, there was tenderness in the epigastrium, although the abdomen was everywhere else soft with no spasm. The aortic impulse was easily palpable and one examiner believed that he was able to elicit definite expansile pulsations in the left lower abdomen. A gastrointestinal series at this time showed a small collection of barium in the duodenal bulb with a slight deformity on some of the spot films. This was thought to represent a niche, and the diagnosis was made of an active duodenal ulcer.

On November 25, 1953, this patient was explored by Dr. Cooper. The duodenum had a questionable scar on its anterior surface just distal to the pylorus, but no active ulcer. In the lower aorta, there was an 8 to 9 centimeter long fusiform expansile swelling which was noted occupying the region of the left lower abdominal aorta just above the bifurcation. It appeared to arise below the renal vessels and was thought to represent an abdominal aortic aneurysm just above the bifurcation. Two aortograms were attempted unsuccessfully by inserting 30 cubic centimeters of 70 per cent solution of urekon into the aorta above the celiac axis. In retrospect, such failure has occurred before with aneurysms which contained large blood clots. As we were not prepared to do a resection of the aorta and it had not been discussed with the family, the patient was returned to his room.

The patient was readmitted on December 14, 1953, at which time there appeared very little change in the aneurysm or his general condition. On December 17, 1953, the abdomen was opened through a long left rectus-splitting incision from the costal margin to the symphysis pubis. Palpation revealed the aneurysm which had been felt previously. After packing the small intestine on one side and the sigmoid on the opposite side, an incision was made in the midline over the aneurysm from the ligament of Treitz to the pelvis. By careful sharp and blunt dissection, the aneurysm was freed and found to go to within 6 centimeters of the renal arteries. After dissection, a tape was placed above the aneurysm just below the renal vein. The aneurysm measured 10 by 15 centimeters and extended down to the right common iliac artery. In order to facilitate handling the aneurysm in case of hemorrhage tapes were placed about the iliac arteries, and clamps next the tapes. A clamp was placed on the aorta immediately above the aneurysm and the aorta was divided. There was very little bleeding. With the aorta divided, it was relatively easy to raise the aneurysm, divide the lumbar arteries coming out posteriorly, and dissect the vena cava from the aneurysm. This dissection was continued until the entire aneurysm was free and the common iliac arteries divided.

A graft was obtained from The New York Blood Vessel Bank, measuring 14 centimeters in length containing the bifurcation and both common iliac arteries. It was prepared and placed in position with the lumbar arteries on top. The proximal aorta was sutured with No. 00000 arterial silk; the suture was started posteriorly and advanced on either side with an everting mattress type suture, and tied anteriorly. With the same material, an over-and-over suture through all layers was placed to approximate the vessel wall further. Thus a very satisfactory closure was effected.

To obtain a good right common iliac artery, it was necessary to remove two additional portions of the vessel; even so, there was some atheromatous material in the wall of the vessel. It was considered best to use the common iliac rather than to ligate the internal iliac artery. This anastomosis was done in a manner similar to that of the aorta. The clamp was released from the common iliac artery on the right after a clamp was placed across the left iliac of the graft, and the graft was seen to fill with blood. The proximal clamp on the aorta was slowly freed and there was an excellent flow of blood passing through the graft into the right common iliac artery.

The left common iliac artery of the patient was sutured to the left common iliac of the graft with the same type suture as used previously, and again blood passed very readily into the left common femoral artery when the clamps were removed. There was very little bleeding.

A sympathectomy was not done. The wound was closed in layers and the patient was returned to his room in excellent condition. At the start of the procedure, the blood pressure was 140/80; at the close, 140/70. The aorta was clamped for 65 minutes. Total time of operation was 6½ hours.

Fig. 5. Case 3. Specimen shows the adherent tumor, which had been resected, together with the adherent great vessels, also resected. The aorta and both common iliac arteries are shown. The longer artery is the left common iliac.

Following operation, there was pulsation bilaterally in the common femoral and posterior tibial arteries. On the left side, the dorsalis pedis was palpable. Pulsation in the dorsalis pedis in the right foot was present but weak. The right great toe was dark, and it was thought a calcium plaque had been freed and acted as an embolus.

Following operation, this patient's convalescence was smooth. He complained of some pain in the abdomen for a time, but this cleared and he was discharged 4 weeks after operation. Five months after operation he feels fine, has very few symptoms, and has good pulsations in all vessels save the right dorsalis pedis.

There have been numerous reports of resection of large vessels during removal of tumors both benign and malignant. These include the carotid, iliac, and femoral arteries. I have been unable to find any report in which the abdominal aorta was included in resection for tumor.

CASE 3. Mrs. S.S., N. Y. H. 625 821, a 57 year old housewife, had a resection of the sigmoid colon for carcinoma 4 years ago. She was admitted to The New York Hospital on May 13, 1952, because of abdominal pain of 7 weeks' duration. A mass, 10 centimeters in size, was present in the left lower

Fig. 6. Case 4. Translumbar aortogram showing complete occlusion of abdominal aorta with enlargement of inferior mesenteric artery.

quadrant. A barium enema showed no evidence of recurrence, although a retrograde pyelogram showed stricture of the left ureter with obstruction above the mass. A translumbar aortogram showed displacement of the aorta to the right, but no actual invasion.

Upon exploration on June 16, 1952, a tumor mass, 10 by 6 by 4 centimeters was encountered lying between the aorta and sigmoid colon. Although not fixed to the deep structures, the tumor was adherent to the aorta and left common iliac artery. It did not actually invade the bowel. The left ureter entered the mass. There were no distant metastases in the liver or lymph nodes along the aorta. The mass was thought to be a local recurrence of the sigmoid carcinoma resected 4 years previously. Exploratory dissection readily freed the tumor from the posterior abdominal wall, but it was found to invade the wall of the aorta. As there was room beneath the renal arteries, the aorta, both common iliac arteries, and left ureter were resected with the tumor. A specimen of terminal aorta with bifurcation and common iliac arteries was obtained from the New York Blood Vessel Bank. After resection of the mass, including aorta, common iliac vessels, and left ureter, an end-to-end anastomosis was performed, and the graft placed between the divided abdominal aorta and both common iliac arteries. The sigmoid colon and left kidney were left in place in order not to subject the graft to the possibility of infection.

Immediately after operation, there was excellent pulsation in the femoral and dorsalis pedis arteries

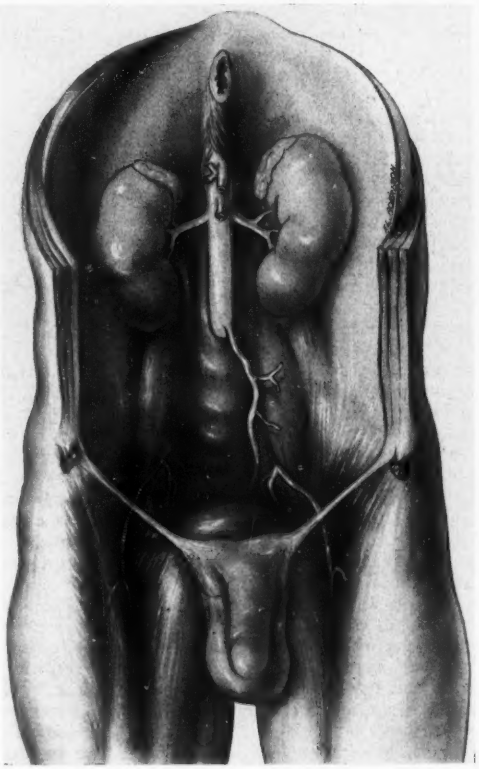

Fig. 7. Case 4. Drawing to show findings at time of operation. Abdominal aorta occluded, both common iliac arteries occluded. Left external and internal iliac patent. Right external iliac and right common femoral artery occluded.

bilaterally. The gross specimen, as well as microscopic sections, showed recurrent carcinoma invading, but not yet penetrating the lumen of the aorta. The patient's recovery was uneventful, and 26 days later the sigmoid colon and left kidney were removed. Carcinoma was present in the resected specimen of the sigmoid.

In addition, this patient had gallstones, an adenoma of the thyroid, and a hernia at the site of an old McBurney scar. Four months later, on October 17, 1952, a cholecystectomy for chronic cholecystitis with cholelithiasis was carried out without incident. Now, 22 months after resection of the aorta, she wants the thyroid adenoma removed and the hernia repaired.

With increased interest in surgery of the large arteries, localized obstruction due largely to arteriosclerosis has been attacked. Intimectomy has been performed on the iliac

Fig. 8. Case 4. Following operation. Graft from distal aorta to left external iliac artery and to left superficial femoral artery.

and femoral arteries, and at times the same has been done in the abdominal aorta particularly when the obstruction has not been complete. However, there is increasing support for the opinion that in occlusion of the abdominal aorta due to thrombosis the vessel should be resected and replaced by graft.

Thrombosis of the terminal aorta has been well described by Leriche. In 1923, he recommended lumbar sympathectomy. In 1949, Elkin advocated resection of the involved aorta. Recent writers have come to the conclusion that the condition is best treated by resection of the involved part and replacement by graft.

Beaconsfield, in 35 cases of insidious thrombosis of the aortic bifurcation, found 28 due to arteriosclerosis. He found the characteristic symptoms to be: (1) extreme tendency to fatigue of both lower extremities; (2) pain in thigh, calf, and ankle; (3) low back pain; (4) loss of sustained erection. On examination, there is loss of arterial pulsation in both legs. He also states that unless treated, these patients will develop gangrene of the extremities. Oudot and Beaconsfield report 5 cases of thrombosis of the distal aorta in which resection and grafting were done. Meillère and Julian prefer to use grafts rather than to remove the thrombus in such cases.

Fig. 9. Case 4. Translumbar aortogram showing patent graft on left from aorta to left external iliac and no filling of graft on right side.

The following patient was subjected to sympathectomy, resection of the aorta, and later to grafting for thrombosis of the aorta. It appears that he would have had a much better result had the graft been applied earlier.

CASE 4. F.B., N. Y. H. 315 795, a 39 year old salesman, was first admitted to The New York Hospital on December 29, 1941. His history dated back 8 months when he developed a dull aching pain in the small of his back on walking. This same pain was present in his left calf and was relieved by stopping or resting for a few minutes. This pain was present only after walking; it was not caused by coughing or straining; it was always relieved by sitting or lying down. The pain was also noticed in the left buttock, and occasionally on the right side. On this admission, there was no mention of palpation of the arteries in the leg. The patient became dissatisfied and signed out against advice

Fig. 10.

Fig. 11.

Fig. 10. Case 5. Aortogram showing marked narrowing of terminal aorta and right common iliac artery with complete occlusion of left common iliac artery.

Fig. 11. Case 5. Aortogram to show complete thrombosis of graft, resulting from bringing iliac vessels out at too great an angle causing kinking of vessels and obstruction.

with a diagnosis of arthritis of the lumbar spine or possible ruptured nucleus pulposus.

He was readmitted to The New York Hospital, 9 years later, October 11, 1950, because of pain in the right hip and buttock. At first, this pain occurred after walking about 5 blocks, but gradually progressed until on admission the same pain occurred after walking ½ block at a fast rate and 1 block slowly. Cold weather caused more difficulty than hot. He had severe cramps in the right foot and tingling sensation in both feet, even while lying in bed, which was not relieved by any change in position. He also noticed that his right foot got cold easily and that there was a constant aching. In addition, he had noticed increasing difficulty in keeping an erection.

On physical examination, there was questionable femoral artery pulsation on the left but none on the right. The politeal and dorsalis pedis pulses could not be felt. The right foot was colder than the left. The lower portion of the abdominal aorta could easily be palpated through the abdomen, and a stethoscope placed over the aorta revealed a loud cystolic murmur. On October 19, 1950, an abdominal aortogram was done by Dr. Howard Dunbar which showed a complete occlusion of the abdominal aorta at its bifurcation. On October 25, 1950, a bilateral lumbar sympathectomy was done by Dr. Dunbar. There was no relief from this procedure.

On November 14, 1950, a resection of the thrombosed distal portion of the aorta, with bifurcation and segments of the common iliac arteries, was carried out by Dr. Frank Glenn. At this operation, it was apparent that directly in the midline overlying the lower portion of the aorta was a rather large vessel that had been visualized in the aortogram. There was considerable induration of the tissue about the distal portion of the aorta from its bifurcation upward for a distance of 6 centimeters. The tissue was edematous with many adhesions and appeared involved in a chronic inflammatory process of long duration. Extending downward along the iliac arteries, there was not so much reaction, but the vessels were smaller than normal and lacked pulsation. Palpation of the aorta above the bifurcation showed it to be firm and solid with a definite plaque on the right side extending slightly posteriorly. The aorta was dissected free, a Blalock clamp placed across it, and the entire vessel divided. In the lower portion was a well organized thrombus. The proximal aorta was closed with 3 rows of silk sutures. Both common iliac arteries were opened and found to contain organized thrombi. There was no back bleeding. These vessels were closed in the same manner as the aorta. Following this procedure, the patient again received no relief. Due to the severe pain, he developed a demerol addiction and was seen in the out-patient department of the hospital on numerous occasions, being examined by the neurosurgeons and psychiatrists in addition to the general surgeons. A cordotomy was offered but this the patient refused.

He was readmitted on April 29, 1953 for consideration of a graft to re-establish circulation to the legs. This time the patient was taking 200 milligrams of demerol every 4 hours and was able to

walk only a few steps. He was having continuous severe pain in both legs, which was described as "charliehorse" in character. On examination, there was no pulsation palpable on either side at any point in the lower extremities. Although the feet were warm there were trophic changes in the skin of the feet with drying and scaling but no ulceration. He was able to move his toes and there was 1 plus edema of the left lower leg. On April 30, 1953, a translumbar aortogram was done which again showed the occlusion of the lower end of the abdominal aorta with a large vessel taking off from this obliterated end. On May 5, 1953, a bilateral femoral arteriogram was done which showed occlusion of the common iliac artery on the left at the bifurcation into internal and external iliac arteries, and on the right side the occlusion continued down the femoral artery to the division into the superficial and deep femoral. We decided to attempt a graft from the occluded aorta to the external iliac on the left and to the superficial femoral on the right side. As there was no graft available, the patient was discharged until such a specimen was found. He was readmitted June 24, 1953. On June 30, 1953, a homologous graft from the aorta to the left internal iliac artery and the right femoral artery was carried out. The abdomen was opened from the symphysis pubis to the costal arch on the left side. The groin on both sides had been prepared with the femoral regions exposed. An incision was made over the femoral artery on the right side and this artery exposed. It was found to be occluded by a recent blood clot, apparently the result of the arteriogram. We were able, by suction, to remove this clot and to get retrograde bleeding from the distal portion of the artery, none, however, from the proximal end. The abdominal incision was opened; there were few adhesions; the distal end of the aorta had been divided just below the inferior mesenteric artery which was quite large and pulsating with a thrill. The distal 1 centimeter of the aorta contained a thrombus. When the left common iliac artery was exposed, it was found to be completely occluded by atheromatous material. There was back bleeding from both internal and external iliac arteries. We thought a graft could be placed from the aorta to the external iliac on the left side and to the superficial femoral on the right side. The defect on the left side measured 16 centimeters and on the right side, 32 centimeters. In order to save the inferior mesenteric artery, an end-to-side shunt was performed on the side of the terminal aorta. A continuous everting suture of No. 00000 silk was used and the proximal end of the graft was placed in the side of the terminal aorta. Following the first row of sutures, another over-and-over suture through all layers was done. A tunnel was made beneath the peritoneum to the external iliac on the left side, and the left branch of the graft was anastomosed in an end-to-side manner into the external iliac as previously done for the aorta. A tunnel was made beneath the peritoneum and beneath Poupart's

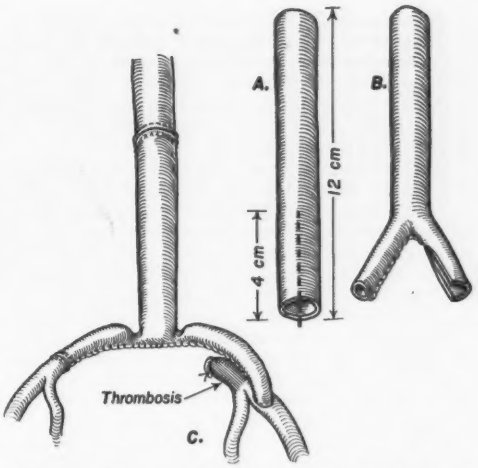

Fig. 12. Case 5. Drawing to show graft. Graft is of thoracic aorta. Bifurcation has been made by splitting aorta and by sutures, making two vessels. Split was not high enough causing vessels to come off at too great an angle, causing kinking and obstruction.

ligament to the superficial femoral artery on the right and an end-to-side anastomosis of a similar character was carried out. This graft was a little short and the anastomosis was made under tension.

When the aorta was slowly released, there was no leakage at any of the suture points. There was good pulsation of the graft and of the external iliac on the left side; however, the femoral on the right did not pulsate. Closure of the abdominal wall was carried out in layers without drainage and the patient returned to his room in good condition. On July 11, 1953, oscillometric readings on the right leg above and below the knee was 0, on the left leg above the knee it was 1.8, and below the knee it was 0.6. A translumbar aortogram, done July 30, 1953, showed the graft on the left side to be patent, and on the right side there was no evidence of dye. Apparently, the entire right side of the graft had thrombosed. In the right leg, there were no pulses palpable in the femoral, popliteal, posterior tibial, or the dorsalis pedis arteries. The leg was cool from the knee down. This patient was last heard from April 21, 1954, ten months after operation. He is still a demerol addict and continues to have pain in his right leg. There are many ulcers of the right leg.

Case 5. O.T., N. Y. H. 72 986, a 51 year old white male, was first admitted to The New York Hospital on October 27, 1953, at which time a diagnosis of thrombosis of the left internal carotid artery was made and a cervical sympathectomy performed on the left side.

He was followed in the out-patient department where he continued to improve regarding symptoms

of the thrombosis of the carotid artery. However, on January 26, 1954, because of pain in the back, x-ray examination showed calcification of the abdominal aorta. At the time, there was no pulsation in the femoral, popliteal, dorsalis pedis, or posterior tibial vessels. The patient was admitted to the hospital on February 6, 1954.

At this time, he gave a history of intermittent claudication of the legs for at least 7 years. This has been severe on walking with cyanosis of the lower extremities on occasions. There has been no swelling, ulcers, or pigmentation. Blood pressure in the right arm was 212/130, in the left arm, 160/100. An electrocardiogram showed numerous changes which were interpreted to be due in part to myocardial changes associated with left ventricular hypertrophy. It also strongly suggested those seen in the evolution of the electrocardiogram following a coronary occlusion of the anterior apex. An aortogram showed extensive arteriosclerosis of the abdominal aorta, and iliac arteries with marked narrowing of the bifurcation of the aorta and complete occlusion of the left common iliac artery. In order to obtain more information about the left iliac arteries, an arteriogram was done. This showed the left common iliac artery to be completely occluded; however, the internal and external iliac arteries were patent. Due to the progressive symptoms, it was thought that this patient was developing a thrombosis of the distal aorta which should be resected and replaced by a graft.

On February 26, 1954, under general anesthesia, a long left rectus incision from the costal margin to the symphysis pubis was made and the rectus muscle retracted. There was no pulsation of the left common iliac artery, the right common iliac artery pulsated, but the posterior wall felt like a rigid stem. The aorta was almost completely occluded in the lower portion. It was believed that in order to help this patient it would be necessary to resect the aorta and both common iliac arteries. The peritoneum was incised over the aorta, both common iliac arteries, and the left external iliac artery. These were visualized and freed. An aortic graft, 12 centimeters in length, was obtained from the New York Blood Vessel Bank. As there was no bifurcation of the aorta available, this being a portion of the thoracic aorta, it was necessary to make a bifurcation. This was done first by ligating all intercostal arteries and splitting the graft for a distance of 5 centimeters anteriorly and posteriorly. Continuous mattress sutures of No. 00000 arterial silk were used to suture the two sides into separate vessels. This suture line was reinforced with an over-and-over suture placed through all layers which gave a very satisfactory appearing aorta with bifurcation. The abdominal aorta was freed for some 5 centimeters above the bifurcation and a clamp was placed about the aorta. Tapes were placed about the internal and external iliac arteries on both sides as precaution to control bleeding. A clamp was also placed across the common iliac artery on the right. As the left was thrombosed, no clamp was used here. The aorta was divided above the area of narrowing and the graft sutured in place with No. 00000 arterial silk. As the right side was patent, it was elected to approach this first. Since there was some back bleeding from both the external and internal iliac arteries, it was elected to do an end-to-end anastomosis to the common iliac on this side. By using the same technique as for the aorta, the anastomosis was accomplished. Unfortunately, there was some kinking of the lower portion of the graft at the bifurcation, and the new common iliac did not pulsate as well as we had hoped, although blood was unquestionably going through the vessel. After close examination, it was thought that the graft should be to the external iliac artery on the left. The same type suture was used with an end-to-side anastomosis from the new iliac artery into the external iliac artery of the patient. There had been marked calcification of the abdominal aorta as well as of the common iliac artery on the right. The calcified intima of these vessels had been removed. It was more difficult to remove the calcium in the left external iliac artery. Again, there was some kinking and little evidence of blood passing through the vessel. It was thought that the result might not be good.

The patient was discharged after an uneventful convalescence and was followed in the clinic. He continued to be somewhat dizzy and his right leg was cold, with pain on walking. The abdominal aorta pulsated well and the right femoral artery could be felt but there was no pulsation. He was readmitted to the hospital for another aortogram, which was done on March 30, 1954, just 4 weeks after resection of the aorta and showed complete occlusion of the entire graft up to an area just below the renal vessels. Sympathectomy was not done as it was thought that such treatment probably would not help this patient. This man should have had an excellent result, and the poor result is due entirely to the graft which was used. The limbs of the graft came off at too much of an angle and kinked both vessels.

SUMMARY

Resection of the abdominal aorta with replacement by graft is the treatment of choice for aneurysm, thrombosis, or invasion of this vessel by malignant tumor. At present, the best replacement is a fresh homologous graft obtained by sterile technique and stored for less than 42 days in balanced salt solution with added serum and antibiotics.

The difficulty in securing such a graft will probably force the use of freeze-dried grafts which have not been obtained by sterile technique and may also permit the use of other than homologous grafts.

Five cases are presented in which the aorta was resected and replaced by a homologous graft. In 2 patients an aneurysm was present. In 2 there was thrombosis of the aorta. In 1 a recurrent carcinoma of the sigmoid had invaded the aorta.

There has been no mortality following this procedure.

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THE EFFECT OF ALTERING ARTERIAL FLOW ON AMBULATORY VENOUS PRESSURE IN POST-PHLEBITIC EXTREMITIES

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ONE of the most challenging therapeutic problems facing the medical profession today is the patient with the postphlebitic syndrome of peripheral edema, pigmentation, and ulceration. The variable results obtained by all methods of surgical treatment emphasize our lack of knowledge of the physiologic factors which produce this crippling condition. Postthrombotic edema has been attributed to venous mechanical obstruction, a combination of venous and lymphatic obstruction, reflux down valveless veins, and to persistent arterial and venous spasm. It is our purpose in this study to consider further the proposition that chronic vasospasm exists in these extremities and to investigate the possibility of improving the venous dynamics by vasodilatation or arterial constriction.

DeCamp and his associates (1, 2), White, and Warren have recently made valuable contributions to our knowledge of venous pressure changes in leg veins of postphlebitic patients under various conditions. It is now well established that venous pressure at the ankle while standing erectly rises to the level of the heart both in normal patients and in patients with obstructed or recanalized deep veins; there is little pressure difference. On the other hand, if a normal patient begins to walk in place, venous pressure rapidly falls to a level between his groin and knee, while the patient with a postthrombotic extremity can seldom lower his venous pressure below the umbilicus or groin by walking at the same speed. Figure 1 demonstrates this difference in walking venous pressures in the two extremities of a patient with unilateral postthrombotic disease. There is a failure to lower pressure by the peripheral pumping action of the leg muscles when the deep vein valves have been destroyed by previous phlebitis.

Attempts have been made to evaluate the effect of various operative procedures, such as deep vein ligation, by observing changes in walking venous pressures before and after the operation. After observing the variability of walking venous pressures in the same vein of the same leg with variation in the amount of edema present from day to day, we believe that it is quite hazardous to assume any base line to interpret the effects of operation. To illustrate, Figure 2 shows the walking venous pressure after prolonged bed rest and elevation of the legs, compared with the pressure in the same leg after 2 weeks' ambulation during which the leg had become moderately edematous. The severe degree of venous hypertension associated with edema suggests that edema of itself adds the element of venous obstruction to a valvular venous incompetence. These observations have led us to measure walking venous pressures as affected by acute variations in arterial inflow in postphlebitic extremities.

METHOD

Henry and Gauer demonstrated considerable variation in walking pressure by simply warming or cooling the extremity; therefore, all experiments were carried out in a controlled temperature room. Mean venous pressures were measured essentially by the method described by DeCamp and associates (1). A plastic No. 7 cardiac catheter was inserted into a vein on the dorsum of the foot or into the long saphenous vein at the ankle. This was connected by a three-way stopcock to a long polyethylene tube attached to a saline manometer. This tube was filled with isotonic saline containing 10 milligrams of heparin per

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liter to prevent blood clotting in the manometer.

The first set of experiments was planned to study the effect of release of arterial spasm on walking venous pressure. Only patients with a definite history of phlebitis were used, and in a majority of them erect venograms had confirmed the absence of normal valves. These patients were studied consecutively and no attempt was made to select or reject patients on the basis of whether or not there seemed to be an element of vasospasm connected with their symptoms. After 1 hour in the controlled temperature room at about 73 degrees F., several basal measurements of walking venous pressure were made with the patient walking at a timed rate and raising his feet 6 inches from the floor. After a reproducible pressure pattern was established, a unilateral lumbar sympathetic block was performed using 10 cubic centimeters of 1 per cent procaine in the region of each ganglion from the first through the fourth lumbar vertabrae. Thirty minutes later, if the foot had shown a definite increase in skin temperature with cessation of sweating, standing and walking venous pressure determinations were repeated. Several patients were eliminated from the study group because there was little, if any, rise in skin temperature after sympathetic block.

In a second group of proved postphlebitic patients, an attempt was made to increase arterial resistance in the leg, simulating arterial spasm, by temporary occlusion of the dorsalis pedis artery. After determining the control standing and walking venous pressure pattern, the dorsalis pedis artery was dissected free through a small incision on the dorsum of the foot, local anesthesia being used. The artery was occluded with a rubber covered bulldog clamp, following which pressure measurements were repeated as before. At the end of the experiment the clamp and venous catheter were removed and these small incisions sutured loosely.

RESULTS

In 9 patients satisfactory increase in skin temperature was obtained after lumbar sympathetic block. In 8 of these extremities the minimum level attained while walking at the standard pace was significantly higher after the block than during the control period. In the ninth patient there was no change. There was a maximum of 19 and a minimum of 5 centimeters in elevation with an average of 14 centimeters in elevation of the lowest pressure attained during walking as compared with the control level. Figure 3 illustrates the pressure profiles of 1 of these patients before and after sympathetic block.

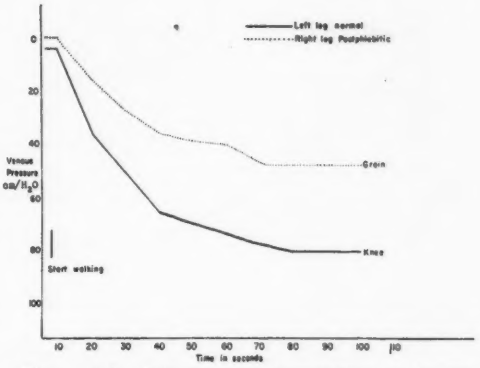

Fig. 1. A.G., July 21, 1953; temperature 73 degrees. Comparison of walking venous pressures in the normal and postphlebitic legs of the same individual.

Five patients were studied before and after occluding the dorsalis pedis artery. In 1 patient (Fig. 4) there was a pronounced drop of 36 centimeters in walking venous pressure after occlusion. In a second patient there was a 5 centimeter decrease in walking pressure; in the other 3 patients there was no change.

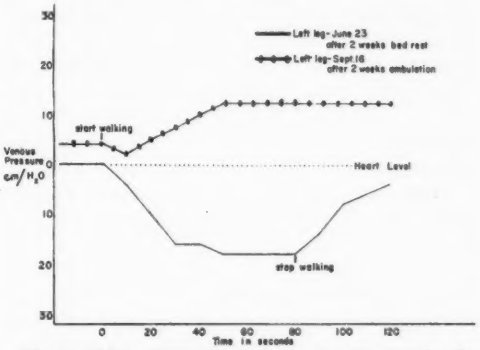

Fig. 2. H.M. Comparison of venous pressures in the same vein of the same leg after bed rest and after prolonged ambulation with edema formation.

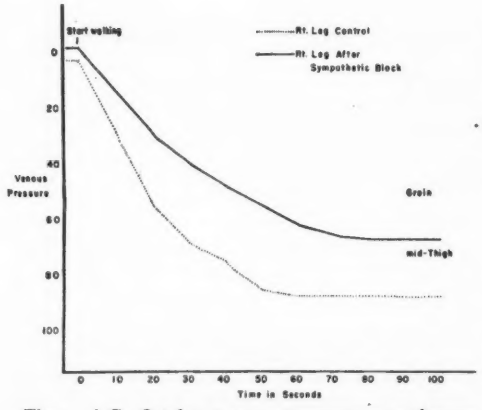

Fig. 3. A.G., October 2, 1953; temperature 73 degrees. Comparison of walking venous pressures before and after effective lumbar sympathetic block.

DISCUSSION

Ochsner and DeBakey have beautifully demonstrated that pain and edema associated with acute thrombophlebitis can be rapidly alleviated by regional sympathetic block. The mechanism of action was shown experimentally to be release of venous and possibly arterial spasm secondary to chemically produced phlebitis. Whether persistent edema after the acute attack has subsided is due to persistent vasospasm is a more debatable problem. A number of surgeons have reported beneficial results from sympathectomy in certain patients with evidence of vasomotor skin changes following phlebitis, but others, notably Linton, have thought that there was no improvement or that in many cases edema and ulceration were made worse by this procedure. Henry and Gauer have suggested that arterial vasoconstriction, if present, might be a favorable circumstance in this condition. They found that in normal adults, during vasodilatation produced by heat, vigorous walking movements failed to reduce the mean venous pressure below 70 millimeters of mercury. When the comfort zone of temperature was reached far less activity was required to effect such a reduction, and when cool, even normal involuntary postural movements would reduce venous pressure to 50 millimeters of mercury. This level approximates that of the counterbalancing osmotic and tissue pressures. It seems most likely, then, that venous pressure in the foot when in the erect posture is a resultant of the relative rates at which blood flows into the veins from the arteries and is removed from them by muscular activity. It has been suggested that this mechanism might account for the fact that edema is often more troublesome in summer than in cool weather.

If there was persistent *venous* spasm in postphlebitic extremities, one would anticipate a reduction in ambulatory venous hypertension after vasodilatation. This did not occur in the studies reported herein and we can find no good evidence in the literature to support the concept of residual venous spasm. The fact that ambulatory venous pressure rises after sympathetic nerve block seems to indicate that arterial dilatation interferes with the effectiveness of the "peripheral venous heart" in these patients by allowing more blood to enter the extremity than can be effectively removed by the defective venous system. Perhaps this accounts for the increased edema occasionally seen following sympathectomy. These deleterious effects on venous dynamics would appear to make sympathectomy unwise in the management of edema and ulceration of the leg, even in the presence of cool, sweaty skin. On the other hand, there has been a very small group of postphlebitic patients with persistent aching pain along the course of the deep veins whom we have been able to relieve in no other way than by sympathectomy. The impression has been gained that theirs has not been a problem of altered dynamics with spasm or edema but a pain reflex from the inflamed veins. In this group, if repeated sympathetic blocks give only temporary relief, sympathectomy has been reluctantly performed in the belief that, despite the relief of pain, circulatory dynamics will be made worse.

The experiments before and after occluding the dorsalis pedis artery were designed to test the postulate that diminished arterial inflow would make walking more effective in lowering peripheral venous pressure. As reported in the foregoing only 2 out of 5 patients showed a walking venous pressure reduction after arterial occlusion. This observation is believed to be due to the fact that collateral circulation around a single obstruction of the dorsalis

pedis artery is so great that no significant decrease of arterial inflow was obtained. This view is supported by the fact that there was a palpable, though diminished, pulsation in the dorsalis pedis below the bulldog clamp in these 3 cases.

In 2 patients with intractable ankle edema so severe that amputation was considered, permanent reduction in arterial flow was evaluated as follows:

CASE 1. At about this point in our studies a 37 year old man presented himself at the Birmingham Veterans Administration Hospital because of severe bilateral ankle edema with ulceration around his right ankle. He had developed a pulmonary embolus in 1946, just 14 days after operation for a ruptured lumbar intervertebral disc. Bilateral superficial femoral vein ligation in the groin was done immediately. Twenty days later he had a second pulmonary embolus following which he was semicomatose for 2 weeks and convalesced very slowly. On ambulation he had severe edema of both legs. In the next 2 years he developed bilateral ankle ulceration, and bilateral lumbar sympathectomies were performed. In 1951 he developed recurrent thrombosis in the right leg. When this subsided the right long saphenous vein was ligated and stripped.

At his present admission he stated that the edema in both ankles and calves to the knee was more massive than he had ever noticed before, despite continuous use of elastic stockings and elastic bandage support. There was a large area of pigmentation and fibrosis around the entire circumference of the right ankle with a 3 by 5 centimeter ulcer on the medial side above the malleolus. The skin of the left leg was much better with only a 3 centimeter area of pigmentation medially. Because of his almost continuous disability from his right leg for 7 years he requested amputation. Before acceding to his request the possibility of permanently increasing peripheral resistance by ligating his pedal arteries was discussed with him. This attempt to reduce his edema by decreasing arterial flow was enthusiastically accepted by him. Therefore, the right dorsalis pedis was ligated with 3 ligatures of silk under local anesthesia. This produced little lowering of skin temperature of the toes and little improvement in his ambulatory edema. Two weeks later the right posterior tibial was also ligated under local anesthesia immediately behind the medial malleolus. Again there was little change in skin temperature and ambulatory edema was not significantly improved. After his ulcer had healed with the aid of a skin graft this patient was discharged to observe the effect of arterial ligation over several months before reconsidering amputation. He failed to return for his scheduled follow-up visits. It was our impression that he received no benefit because of the very good collateral circulation evidenced by the skin temperature of his feet.

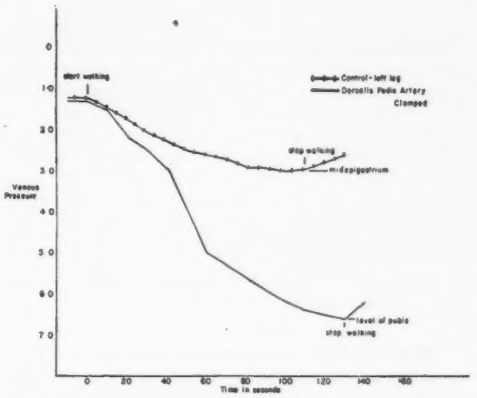

Fig. 4. C.J.B., September 10, 1953; temperature 73 degrees. Comparison of ambulatory pressures before and after temporary occlusion of the dorsalis pedis artery.

CASE 2. A 29 year old man was kicked in the ankle in a fight 1 year before admission. The entire leg to the knee became swollen and painful, and he was admitted to a hospital the next day. The pain and swelling gradually subsided, and he was treated during the same admission by multiple ligations of the left long and short saphenous vein for varicosities which he had developed. After discharge he was seriously disabled by massive edema of the leg extending above the knee. He was not able to prevent this edema by careful use of an elastic bandage. After almost continuous hospitalization for 1 year because of this leg, he was transferred to the Veterans Administration Hospital, Birmingham. There was beginning pigmentation and fibrosis above the left medial malleolus but no ulceration. There were no superficial varicosities. Because of his persistent disability with no sign of improvement, this patient was beginning to consider the possibility of amputation. Ambulatory venous pressure studies were carried out before and after temporary dorsalis pedis artery occlusion. In this patient a marked drop of 36 centimeters occurred after occlusion (Fig. 4). In view of the lack of ischemic change in the foot of the patient in Case 1 after ligation of his pedal arteries, and because of the favorable response to occlusion of the dorsalis pedis alone in this patient, permanent ligation of both pedal arteries was considered. This patient was also enthusiastic and co-operative after a careful explanation of what we were trying to accomplish was given him, including the dangers of ischemic complications. Under pentothal anesthesia the dorsalis pedis and posterior tibial arteries were dissected out at ankle level and permanently ligated with 3 silk ties each but not divided. The dorsalis pedis artery was found to be about twice normal size and the posterior tibial very small. This almost certainly accounted for the greater drop in ambulatory venous pressure after dorsalis pedis occlusion in this man

than in any of the other patients. A much larger percentage of the total blood supply to his foot was entering through the dorsalis pedis than usual. After permanent arterial ligation, the left foot was cool for 2 days, then rapidly returned to its normal temperature. At the end of a week a feeble pulse could again be felt in the dorsalis pedis below the site of the ligatures. This could not possibly have been recanalization and certainly indicated dilatation of the collaterals around the point of obstruction. One week after ligation when he became ambulatory there was slight improvement in the amount of edema after short intervals of standing, but it was soon evident that there would be little permanent lessening of the edema following this procedure.

Although these patients failed to be benefitted by ligation of the pedal arteries, it was apparent that rapid development of collateral circulation precluded any effective diminution of arterial inflow. It seems certain from the experimental evidence that the thesis is sound, but there is no immediate encouragement for further clinical application of the principle of arterial insufficiency to reduce peripheral venous hypertension.

SUMMARY

The variation in ambulatory venous pressure in postphlebitic extremities due to temperature variations and degree of edema is discussed.

Acute experiments in 9 postphlebitic legs before and after lumbar sympathetic block demonstrated that arterial vasodilatation made walking less effective in lowering peripheral venous pressure in 8 of these. This was thought to explain the increased edema often noticed in warm weather and in some post-thrombotic extremities after sympathectomy.

Attempts to improve the effectiveness of ambulation in reducing venous hypertension by temporary occlusion of the dorsalis pedis artery were successful in only 2 out of 5 patients.

Two attempts to reduce massive intractable edema following phlebitis by ligating permanently the dorsalis pedis and posterior tibial arteries at the ankle were clinical failures. This result was believed to be due to the adequacy of collateral circulation at the ankle, so that arterial ligation did not sufficiently reduce flow into the foot.

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INDICATIONS, ADVANTAGES, AND SURGICAL TECHNIQUE OF VAGINAL HYSTERECTOMY

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IT is not our intention in this presentation to enter into a discussion of abdominal hysterectomy versus vaginal hysterectomy but we do propose to emphasize the advantages of vaginal hysterectomy for correction of some gynecologic lesions. We shall attempt to do this by an analysis of all cases (401) in which treatment was by vaginal hysterectomy in 1952, and we shall compare them with cases of the 7 previous years (1946 through 1952).

The historic data given by Kennedy and Campbell, relating to the origin, development, and extension of vaginal hysterectomy are worth study. Heaney, who has done much to make this procedure generally accepted in this country, has pointed out that the earlier gynecologists (Emmett, Sims, Skene, Henrotin, and Price) always removed the uterus by the vaginal route, except under exceptional circumstances, since laparotomy, in their time, carried a much higher risk. With the development of aseptic surgical measures, pelvic lesions began to be attacked by the abdominal route and vaginal hysterectomy, except for extreme procidentia, was done much less frequently. Therefore, a considerable time elapsed when little was taught on vaginal hysterectomy and it was seldom discussed. The trend has been changing during the past few years. This perhaps is partly due to the interest in vaginal surgery in general, as emphasized by Allen (1, 2). Certainly any surgical procedure which is corrective in nature and by which diseased parts are removed with reduced risk and disability, should be familiar to all who are doing pelvic surgery (3).

The number of patients treated at the Mayo Clinic by vaginal hysterectomy since 1945 has remained about the same each year. During the past 7 years, the total number has been 2,867, with only 1 death. This was of a patient, aged 62 years, who died on the twelfth postoperative day from bronchopneumonia and uremia. There have been no deaths since 1948, which we believe is a satisfactory index of the safety of the operation, especially when it is considered that some of these patients are more than 60 years of age.

The year 1952 (previously mentioned) is the last one for which our statistics are yet complete. What was done for the patients of that year, in general, would be the same as for those of all previous years.

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AGE

The incidence by age was as would be expected: 11 cases in the 20 to 29 year age group, 51 between 30 and 39 years, 128 between 40 and 49 years, 103 between 50 and 59 years, 95 between 60 and 69 years, 12 between 70 and 79, and 1 between 80 and 90. The majority of the patients were between the ages of 40 and 60 years but some were younger. The uteri of these younger patients were removed for uncontrolled bleeding after intensive treatment had failed to halt it.

PARITY AND MARITAL STATUS

Parity is of interest only in that the majority of the patients had had children. Thirty-three patients were nulliparous, 368 were parous; 9 were unmarried and 392 were married. The facility of the operation is not related to parity, as some may think. Generally, it is just as easy, and often safer, to operate on the nulliparous than on the multiparous patient, since the bladder, ureters, or posterior cul-de-sac of the former has not become scarred or distorted. Many of the multiparous patients may have had one or more previous vaginal surgical procedures for cystocele, prolapse, or incontinence during their active reproductive period, resulting in scarring, vaginal shortening, or partial stenosis and fixation,

TABLE I.—INDICATIONS FOR SURGERY

	No. cases
Incompetent vaginal support	132
Incompetent vaginal support plus urinary incontinence	61
Incompetent vaginal support plus recurrent incontinence	4
Incompetent vaginal support plus abnormal bleeding	65
Incompetent vaginal support plus uterine myomas	15
Abnormal bleeding with or without fibroids	69
Dysmenorrhea	7
Carcinoma of endometrium	5
Carcinoma of cervix in situ	42
Basal cell hyperactivity of cervix	1
Total	401

producing conditions which cause vaginal hysterectomy to be much more difficult to do. However, on account of recurring incontinence, high rectocele, or colpocele and menopausal menorrhagia, this type of operation is definitely indicated rather than an incomplete vaginal operation or a combined abdominovaginal procedure, which a few years ago was a common occurrence. There were 33 of these women who had not had children. Nine of these were spinsters.

Previous abdominal operations are, we think, of considerable importance especially since this factor might affect the conduct of the operation. For example, a patient may have undergone some type of uterine suspension at one time and now years later she may present the clinical picture of uterine prolapse, but in reality she has a greatly elongated cervix. The uterine fundus may be fixed to the abdominal wall or to her intrapelvic structures, causing the vaginal hysterectomy to be considerably more difficult. Also, the cul-de-sacs can be obliterated either by scar or by disease, which increases the risk of injuring the urinary structures or the adherent bowel. Such situations should not contraindicate a vaginal hysterectomy if it is definitely indicated, but they serve only as danger signs during the conduct of the operation.

Among the results of previous vaginal operations which can often be troublesome is the multiple scarred and short anterior vaginal wall where the bladder is fixed to it or as it often seems, has become an intimate part of the vaginal wall. The bladder can be separated only by sharp dissection. In most of such instances the bladder has to be separated from the pubic rami as well as from the anterior surface of the uterus.

It is surprising to find in many patients requiring vaginal hysterectomy extensive scarring of the perineum, which is fixed, producing dyspareunia, and is still inadequate as far as perineal and rectal support is concerned. In such situations these perineums have to be cut down or in reality, excised before the vaginal hysterectomy can be undertaken. Scars may extend up either lateral vaginal wall and into the base of the broad ligaments. Careful measurements must be instituted before one proceeds with the operation so that the reconstruction will result in as nearly normal a vagina as possible with adequate depth and diameter. Seventy-seven of these patients had had previous gynecologic abdominal operations and 37 had had one or more major vaginal surgical procedures.

INDICATIONS FOR SURGERY

The indications for vaginal hysterectomy are being extended gradually, and we are sure that this is a very distinct advantage for the patient. Not so many years ago, uterine prolapse was the chief reason for vaginal hysterectomy, and in the minds of many pelvic surgeons it was the only true indication. However, there are several other clinical entities associated with prolapse or incompetent vaginal support, such as primary urinary incontinence or recurring incontinence, abnormal bleeding and uterine fibroids, which are more satisfactorily managed by instituting vaginal hysterectomy. Incompetent vaginal support does comprise the greatest number of these cases (Table I). There were 69 patients with abnormal bleeding with or without uterine fibroids, who underwent vaginal hysterectomy. It was this group of patients that formerly we were accustomed to treat by the application of intrauterine radiation, but we consider now that surgical removal of the uterus vaginally with preservation of normal adnexa in the premenopausal patients is a much better service to the patient. The postoperative disability is so insignificant in comparison to the benefits to the patient that we

think this method of treatment is justified in such instances. For the same reason, certain types of dysmenorrhea are best managed in this fashion. We treated intractable dysmenorrhea in 7 cases in 1 year by this method.

Occasionally we treat carcinoma of the endometrium by vaginal hysterectomy. This is done only on very select patients and for very good reasons. Such patients are quite obese, hypertensive, and may have already experienced some slight vascular accident with or without clinical residual evidence. These patients are always multiparous with incompetent vaginal support. Here, just as radical an operation can be done vaginally with removal of both adnexa as could be done abdominally except for dissection of lymph nodes. In such patients dissection of lymph nodes certainly would hardly be justified anyway. Repair of a cystocele or rectocele, which most of such patients have, is not done at this time on account of the possibility of implantation of malignant cells.

We are of the opinion that many patients with carcinoma of the cervix in situ or stage 0 are best handled by this method. When positive smears and biopsy confirm the presence of a malignant lesion and it is thought to be in situ from the biopsy, a complete conization is performed to include all the endocervical glands. If immediate pathologic inspection does not reveal any invasion and the patient has her family, we perform vaginal hysterectomy. If a study of the cervix by serial section reveals any invasion then the parametrium and obturator and iliac lymph nodes are removed subsequently. There were 42 patients so treated in this 1 year series. Further discourse on the management of carcinoma stage 0 is not within the scope of this analysis.

SURGERY PERFORMED

The extent of surgery performed when vaginal hysterectomy is indicated is of interest in that sometimes patients do not need anything done except removal of the uterus. Some may need only repair of the anterior vaginal wall or a plastic repair of the vesical neck for incontinence. Occasionally, there is no cystocele or incontinence but a high rectocele and and incompetent perineum. Inspection of the adnexa is imperative in each case, and the adnexa can be resected or removed as may be indicated (Table II).

TABLE II.—OPERATION PERFORMED

	No. cases
Vaginal hysterectomy only	79
Vaginal hysterectomy plus anterior repair	11
Vaginal hysterectomy plus posterior repair	47
Vaginal hysterectomy plus anterior and posterior repair	206
Vaginal hysterectomy plus adnexal removal (one or both)	13
Vaginal hysterectomy plus adnexal removal plus anterior or posterior repair or both	45
Total	401

SPECIAL PROCEDURES REQUIRED

There are associated surgical problems in connection with vaginal hysterectomy and plastic repair that can be of serious importance and should be emphasized in any discussion on this subject. For example, morcellation of fibroids may be required before the uterus can be delivered. Submucosal fibroids may be of sufficient size that hemisection of the uterus will be necessary in order to extract one or more fibroids so that each segment of the uterus can be delivered. Pedunculated fibroids do not usually present as much difficulty as do the submucosal ones.

A rigid perineum or a scarred fixed perineum may offer considerable difficulty to the proper approach so that a generous episiotomy will facilitate the procedure considerably.

When a patient has had multiple pelvic operations resulting in rather dense attachment of the bowel to the uterine fundus, it is often most difficult to separate them without producing an opening in the bowel. This is particularly true if the ovary is attached to the intestine. These openings must be looked for and immediately repaired transversely. Small intestine can be resected through the vagina if the mesentery is sufficiently mobile. However, one should never hesitate to do a laparotomy if it is at all required.

Injury to the bladder is a rare accident in our hands, having occurred once in this series (Table III). It is most likely to occur in those patients who have had previous repair of cystocele or interposition operations. If the bladder is empty, an injury of the vesical wall

TABLE III.—SPECIAL PROCEDURES REQUIRED

	No. cases
Morcellation of fibroids	5
Hemisection of uterus	6
Episiotomy	2
Resection of bowel or repair of intestinal injury	3
Repair of vesical injury	1
Excessive bleeding requiring transfusion during procedure	34
Ovarian resection	17
Special operation for incontinence	45
Partial or complete vaginectomy	5

can be easily missed. Some surgeons keep a colored solution or just plain water in the bladder in order that any opening of the bladder can be seen at once. There is no other tissue which resembles bladder, so that if one constantly observes the character of the tissue being cut there should be fewer injuries of the bladder. Any repair required is best done transversely.

Many patients will require transfusion during the operation, since some may have a severe secondary anemia from bleeding fibroids or functional bleeding. Too, patients who are obese, with prolapse or who have had previous phlebitis will have some large veins or varices in the vaginal wall and broad ligaments. Such patients may lose a pint of blood during the surgical procedure, since it is not wise to attempt to clamp and tie all these varices because too much valuable time is consumed. It is obvious then that the blood of each of these patients should be typed and grouped before the patient goes to operation. The value of a transfusion in patients who have had considerable loss of blood before operation can hardly be overestimated. Their convalescence is considerably improved and shortened.

TABLE IV.—PATHOLOGIC CHANGES PRESENT

	No. cases
Myomas	107
Hypertrophied uteri (more than 120 gm.)	56
Endometriosis or adenomyosis or both	27
Carcinoma of endometrium	6
Carcinoma of cervix in situ	31
Endometrial polyps	27
Ovarian pathology	
Dermoid cyst	2
Cystadenomas	3
Endometriosis	4
Simple cysts	25
Pyometra	2
Atrophic uteri (normal)	166

In the younger group of patients in whom it is desirable to preserve the adnexa, one may encounter fairly sizable cysts, of endometrial origin, follicular origin, or dermoids. These cysts can be resected in most instances with preservation of sufficient ovarian tissue equal to a normal ovary. This, we believe, is justified in these patients but in the menopausal group such adnexa should be removed.

Incontinence of urine is an associated situation, especially in the multiparous patient, which seems to us to require much consideration. So many patients fail to relate this difficulty unless they are questioned concerning it. When there is incontinence it is necessary to know the type, such as postmenopausal, postoperative, or neurogenic. The operative procedure to correct it can vary considerably in extent depending on its severity. Simple plastic operations on the vesical neck and urethra will cure 75 to 85 per cent if the normal urethrovesical angle is restored. To restore this angle in patients who have had one or more previous operations for the same thing requires more extensive procedures than the usual mattress sutures or the Kelly stitch. In this group there were 45 who required some special surgical procedure to adequately correct their incontinence.

It should also be noted that not all patients with severe prolapse and cystoceles have also urinary stress incontinence. But, unless the critical urethrovesical angle is restored during the process of vaginal hysterectomy, the patient will have postoperative incontinence.

PATHOLOGY

Quite obviously in patients with procidentia and in many patients with functional bleeding the uteri will appear as essentially normal. There were 166 atrophic uteri which we designated as normal (Table IV). All uteri that were without fibroids but that weighed more than 120 grams we considered as hypertrophied, or some were designated as "subinvoluted or wet uterus" in our surgical dictation. In 107 cases there were 1 or more uterine fibroids.

As a general rule, patients with clinically demonstrable endometriosis are not selected for treatment by vaginal hysterectomy. When

this lesion was found it was incidental or a complicating lesion with multiple small fibroids. Uterine prolapse of any degree is rarely seen in the presence of endometriosis. When this lesion is encountered in the cul-de-sac it is rarely necessary to repair the vaginal wall, because the lesion itself produces sufficient scarring and fixation.

It is of interest that in several cases of carcinoma in situ, the entire lesion was removed with the biopsy or the conization so that no more of the lesion was observed in the laboratory after the uterus was removed. This is valuable information particularly if this lesion occurs in a young person who desires more children.

The ovarian pathologic changes comprise dermoid cysts, cystadenomas, endometriosis, and simple cysts. Obviously many of the ovaries were also atrophic.

POSTOPERATIVE COMPLICATIONS

The type and number of postoperative complications are about what one should expect in this type of surgery. These are directly related to the extent of the vaginal repair required. There are rarely any postoperative complications when just a vaginal hysterectomy is done. We believe that certain complications are unavoidable especially when one reconstructs the vesical neck for recurring urinary stress incontinence. In many instances it is necessary to overcorrect it, which usually is associated with edema of the mucosa of the trigone and internal urethral orifice. Thus these patients will experience urinary retention (Table V) which rarely lasts beyond the fourteenth postoperative day but we have seen it last for 3 weeks. Urinary retention may, in part, be due to a painful perineum, especially if considerable scar has been excised prior to performance of perineorrhaphy. When the perineum is indurated and painful the patient cannot relax the urethral sphincter when extensive vaginal repairs have been performed together with vaginal hysterectomy. We believe it is far safer to keep a Foley catheter in the bladder for 10 days or longer if necessary. After the catheter is removed, the patient is catheterized twice a day for residual urine. This is continued until the residual urine is 30 cubic centimeters or less before the patient can be dismissed from the hospital.

TABLE V.—POSTOPERATIVE COMPLICATIONS

	No. cases
Urinary retention	59
Pelvic infection	29
Pelvic abscess or hematoma or both	7
Bleeding	6
Anemia requiring transfusion	8
Thrombophlebitis	3
Gross hematuria	2

Infection is not a serious complication. When it does happen it usually is due to an infected hematoma located between the peritoneum and the vaginal wall. Intrapelvic infection is most unusual. Infection is indicated by continued fever for 4 to 5 days, at the end of which period drainage usually breaks through the path of least resistance which is into the vagina. A hematoma may extend into the broad ligament or infiltrate along the adnexal ligament. This has never required evacuation or exploration abdominally.

Bleeding is one factor that is unpredictable and usually occurs about the time the catgut sutures are releasing. This is often related to coughing or straining at defecation. Resuturing is not often required. A gauze pack for 48 hours is usually sufficient. When bleeding continues, the vaginal canal should be inspected under direct vision in the operating room. Blood in the urine does not always signify injury to the bladder. This can come about by rupture of a small vein near the trigone when the Foley catheter is inserted. The hematuria subsides in a day or two.

NUMBER OF DAYS IN HOSPITAL

Patients who have a short stay in the hospital are those who have only a vaginal hysterectomy. Seventy-three were hospitalized 6 to 8 days, 183 from 9 to 11 days, 88 from 12 to 14 days, 27 from 15 to 17 days, 15 from 18 to 20 days, 13 from 21 to 30, and 2 more than 30 days. Those patients who had to remain longer than 11 days were those who had vaginal repairs plus those who had more extensive operations for their stress incontinence. As we observe this situation we doubt if this percentage of delayed hospital stay can be

reduced if one is to be sure that the incontinence is cured.

COMMENT AND SUMMARY

When one reviews an analysis of a group of patients who have undergone one or more surgical procedures designated as vaginal surgery, there are certain points that immediately present themselves for further discussion and perhaps clarification.

Selection of patients for vaginal hysterectomy should not be difficult, although some surgeons might disagree with the indications as shown in this analysis. The statement that it is better to perform abdominal hysterectomy for small fibroids because one wishes to remove the appendix or explore the small intestine or the structures within the upper part of the abdomen is no longer tenable. The refinements in clinical investigation nowadays can, with quite reasonable accuracy, tell us if structures as outlined are within normal limits or not. Further, it is not considered good practice to combine upper abdominal surgery with lower abdominal surgery or vice versa. Also, we do not regard it as good practice to struggle to extract large fibroids through the vagina. However, occasionally one gets a surprise and finds that the tumors are larger than clinically expected. In such a situation one certainly should not hesitate to discontinue the operation and proceed by the abdominal approach. Personally, one of us (Counseller) has never had to do this but would not hesitate if the situation demanded it.

Functional bleeding is a condition which can be very satisfactorily treated by vaginal hysterectomy. Careful selection must always be done, especially in the younger patient. In them vaginal hysterectomy is performed only after all other medical treatment has failed and the patient must have relief from constant loss of blood. Adnexa that are normal in these patients should be preserved. The premenopausal and menopausal menometrorrhagia lends itself well to this type of treatment. We prefer this as a general rule to intrauterine radium therapy. There is the occasional case, however, in which radiation therapy is preferable if vaginal hysterectomy would be difficult. So often the patient can be made much more comfortable by hormonal treatment for her menopausal symptoms and bleeding so that we believe she can be more adequately and safely treated if the uterus has been removed vaginally.

Oophorectomy we believe should be discussed more and perhaps performed more than actually has been done. The menopausal patient is the one we have reference to. Subsequent carcinoma of the ovary is a tragedy because it is a silent disease and when discovered it is usually inoperable. It occurs sufficiently often that we have come to believe that routine oophorectomy in that group would not be a mistake. It is necessary to discuss oophorectomy with the patient before operation is undertaken so that there is no misunderstanding. Some patients may refuse oophorectomy if the ovaries appear normal at the time of operation, and we think their wishes should be respected if they have been made familiar with the facts.

We are of the opinion that the fear of hemorrhage does deter some surgeons from performing vaginal hysterectomy when it is clearly indicated as the best surgical procedure for the particular patient. This situation actually should not be when one is quite familiar with the anatomy and the major blood supply of the pelvis. This difficulty should occur only when the blood supply is distorted from interligamentous fibroids or ovarian cysts. Here, also if the ovarian pedicle should retract so that the surgeon could not reach it, then it is no problem to open the abdomen if necessary. When branches of the uterine artery retract, the bleeding may seem formidable and these can usually be picked up with the long finger forceps and clamped with the Haney clamp or a long curved forceps. The only important technical maneuver is to clamp only the bleeding vessel and to avoid including the edge or side wall of the ureter which usually is not far away. Stick ties in this region are also dangerous for the same reason. Primary ligation is much safer.

Postoperative bleeding can be troublesome but rarely critical. It is critical only when the ligature or stick tie loosens or slips off of the uterine pedicle, which is usually about the

time the patient is ready to leave the hospital. Since this does sometimes happen we routinely doubly ligate the uterine pedicle just the same as we do when an abdominal hysterectomy has been performed. We recommend this as a safety maneuver. Postoperative bleeding from the anterior or posterior suture line is not so critical and is usually controlled by a gauze pack. If it is seen to be arterial bleeding, then a mattress suture may be required.

In conclusion we have presented an analysis of data on 401 patients who underwent vaginal hysterectomy and the associated surgical procedures during one single year. The number of patients who we believed would be best treated by this operation has remained about the same during the past 7 years, during which time 2,867 were so treated with only 1 death. Pertinent points regarding the selection of patients and technical problems have been discussed.

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EDITORIALS

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DECEMBER, 1954

THE CHANGING STATUS OF THE SURGICAL TREATMENT OF TUBERCULOSIS

NO FIELD of medicine or surgery has undergone more remarkable changes in the past decade than the treatment of pulmonary tuberculosis. Once a well organized plan of therapy giving quite favorable results, it has now been so altered in almost every facet as to be almost unrecognizable. Tried and proved techniques, pneumothorax, and thoracoplasty, once considered of the greatest value, have been abandoned or discarded as old fashioned and have been superseded by others of greater apparent worth. Clinical results at one time believed excellent are now, under more rigid criteria, considered inadequate and incomplete in comparison to those which may now be accomplished.

Several agents which singly could not have drastically altered the situation have, in proper combinations, produced revolutionary changes. Specific antimicrobial therapy, improved anesthetic agents and procedures, banked blood, improved surgical techniques, and a better understanding of the segmental anatomy of the lung have each contributed its share. The Shakespearean approach to the problem as expressed in Lady Macbeth's "Out damned spot" has always had its appeal to the surgeon-phthisiologist, but only recently has its relatively safe accomplishment become possible. Tuffier in 1891 successfully excised a tuberculous mass from the apex of the lung. Subsequent attempts, however, were less successful and surgeons who later excised tuberculous lung lesions inadvertently or intentionally were deterred from repeating the procedure very often by unpleasant complications which followed all too frequently.

The removal of a major destructive tuberculous focus is fundamentally better than its immobilization by any known means if the price paid be the same or less. Reduction in risk and the incidence and severity of complications have now reached the point where many major or even heroic procedures—pneumonectomy, pleuropneumonectomy, and decortication—may now be quite routinely accomplished at a reasonable price. There can be little argument concerning the advisability of resection of destroyed areas of lung, obstructed and suppurating areas, bronchiectatic and bleeding segments, and larger caseous areas, or the fact that their elimination improves the patient's chances of recovery.

The present program of rest and chemotherapy with two drugs to maximum improvement (target point) provides an excellent rule of thumb for consideration of resection for the larger lesions but not for the smaller

ones. Failure of a cavity to close or the sputum to convert may provide as good an indication for a change in chemotherapy as for resection, since lack of response may be evidence of emergence of resistance of the offending organism to the drugs in use.

Tomographic studies for residual disease or cavity are at times of great help although they are not altogether reliable. Not infrequently, a study of the original roentgenograms may give a better indication of the disease to be encountered at the time of surgery than a study of the more recent films or tomograms.

Conservation of pulmonary function in all resections, especially in extensive or bilateral disease, should ever be our goal if the patient is to be rehabilitated to a useful existence. This is another advantage of resection over any collapse procedure.

The handling of the smaller foci presents a greater problem. Enthusiasm for the new procedures and the relatively insignificant risk of removal of the smaller lesions have unquestionably led to many unnecessary resections. Surgical removal of all tuberculosis from any patient's body is physically impossible. There can be little satisfaction and perhaps less virtue in the excision of fibrotic residues, scars, small fibrotic tubercles, or well encapsulated foci containing few or no bacilli of questionable or unproved viability or virulence. The human body has always possessed potential or established ability to control the smaller tuberculous foci. This may be enhanced and extended to more extensive lesions with the aid of chemotherapy. The increasing evidence of the progressive effects of very prolonged chemotherapy certainly should remove the necessity for many of the smaller resections.

The earlier complications encountered are directly related to bacterial resistance, to section of bronchus or lung through active tuberculous disease, to failure to obliterate pleural space and to residual pleural fluid pockets. The later complications are more closely related to localized pleural infection (empyema), to bronchial fistula and retained bronchial suture material than to exacerbation of parenchymal disease.

The impact of the present treatment of pulmonary tuberculosis by chemotherapy plus resection is becoming evident in the sanatoria of the country. Vacant beds resulting from a shorter stay, earlier discharge, and fewer readmissions are now the rule rather than the exception but as yet, there has been less reduction in the number of new patients admitted. Favorable as the picture now appears to be, it is still changing and the ideal treatment of today may not be the best treatment of tomorrow.

Many unknowns remain to be solved in the years to come. Do patients under present treatment develop their own resistance against tuberculosis sufficiently to protect them against the future onslaughts of this organism after the effects of chemotherapy have worn away? Are the organisms at present submerged by chemotherapy really dead or merely hibernating to awaken subsequently and again start their destructive process? Are we keeping our patients in bed too long or long enough?

How long may chemotherapy be continued and how long must it be continued? How far may we go with ambulatory chemotherapy before or after resectional therapy? Can new antibiotics be developed rapidly enough to keep ahead of the emergence of resistant organisms in some individuals? What is the fate of the individual who becomes infected with organisms already resistant to our present drugs? Will our present plan prove as ineffective in the long run as did the short-

term chemotherapy program of a few years ago?

Are the results of our present treatment as good as they seem or have we merely evaluated them too early?—a notorious pitfall in treating tuberculosis. Might not some of the older forms of therapy, now in the discard, prove equally as valuable as the new with chemotherapy available to reduce many of the complications previously encountered? Are our present criteria of clinical results too strict? How significant is an occasional positive gastric culture in the absence of demonstrable cavitation or significant lesion, and how dangerous is it to the patient or those about him? How many of our present patients now so blithely discharged with negative cultures while yet under chemotherapy will in the future be found to be positive after the effects of chemotherapy have been dissipated? How efficacious can chemotherapy be in the mass control of tuberculosis in other sections of the globe where it is so prevalent?

To none of these questions are the answers apparent at this time. Much has been accomplished but far more remains to be done before the "Captain of the Men of Death" is banished from our midst.

THOMAS J. KINSELLA.

WISHFUL THINKING AND THE CANCER PATIENT

IN THE last 10 to 15 years the surgeon has assumed an increasingly important role as the individual mainly responsible for the patient afflicted with cancer. This is primarily due to two factors, namely, the more accurate definition of the areas of usefulness of radiation therapy, and consequent contraction of its field of application, and, secondly, the expanding possibilities of excisional surgery. The average qualified surgeon today routinely accomplishes surgical procedures that only a few pioneers had the temerity to initiate in the relatively recent past. Our improvements in surgical techniques, and diminishing mortality rates, have led to such feats of physiologic rearrangement that some have suggested that surgery has progressed past the point of human usefulness in certain situations. Conversely, it has also been remarked that surgical progress against cancer has consisted of cutting an inch wider and deeper each year, until we are sometimes through into the mattress, without compensatory increase in cure rate. With surgery for the moment in ascendancy in the precarious and constantly shifting balance of the modalities used to treat cancer, it would seem to be a good time to evaluate our position.

The bulk of cancer surgery is not done in the well recognized large clinical and teaching centers in this country, but, on the contrary, the vast majority of cancer patients are treated at the community level. This is as it should be, and this level of care is constantly being raised because of the surgical training programs which are turning out hundreds of qualified surgeons each year, all of whom, obviously, cannot be retained on the staff of their parent institution. This trend has mitigated to some degree one of the great American surgical fallacies, to wit, that any individual surgeon's cancer cure rate is automatically as good as that reported from the best centers, if his immediate surgical mortality is comparable to theirs. Human nature being what it is, even at the professional level, it is much less painful to sign a death certificate 2 years after resection of a cancer of the colon than on the sixth postoperative day. Failure to cure in such a situation is too frequently unavoidable, in which instance we have at least allowed a patient a year or so of functional life, rather than death in a few

weeks from intestinal obstruction. Perhaps equally frequently, however, a cancer death could have been prevented by performing a left hemicolectomy, rather than excising a 6 inch segment of bowel because the anastomosis is easier. The ability successfully to anastomose a cut loop of dog's gut does not constitute cancer surgery.

To the careful and sentient surgeon technique is of fundamental importance, but by now it should be accepted as a basic requirement from which we should reach to higher planes of responsibility for the cancer patient. Constant attention to diminishing mortality and morbidity rates should be taken for granted, and our sights raised from the patient's hospital stay to his condition 1, 2, and 10 years from the time of surgery.

The diagnosis and definitive treatment of the cancer patient is, on the whole, the most responsible function of the surgeon. Cancer is one of the only diseases the surgeon is called upon to treat which is essentially 100 per cent fatal untreated. In theory, death from cancer should be, to a large extent, preventable, but in actuality we fall far short of the estimated salvage. One of several important reasons for this is the diffusion of responsibility for the patient. The surgeon may see the patient only during his hospital stay, and in office visits for a few weeks thereafter. A doctor who knows far more about measles, diabetes, and obstetrics than the surgeon, but far less about cancer, then takes over. Or, and equally relevant, the patient may want no part of follow-up visits, preferring to forget the whole thing, thus refusing his own portion of responsibility for himself. Parenthetically, a number of cured cases are lost for evaluation this way. At any rate, too often the cancer patient winds up at loose ends, and when recurrence takes place he and his family begin to "shop around." The recurrence may not become apparent until months or years after the critical period of definitive treatment, so that when finally a failure of cure is brought to the surgeon's attention, if ever it be, time has so attenuated the impact that he is inclined to philosophize that "no one can cure all cancer," and this is "just one of those cases." If recurrence and death from cancer were immediate and dramatic, our sense of personal responsibility would be kept taut, but the time lag in the disease allows slackening, so that too often the surgeon takes the line of least resistance from the beginning, instead of the line of *most* resistance. The serious treatment and evaluation of cancer patients is a grim business, and not too many men are willing to do the follow-up in other than a casual fashion. Personal experience is an enlightening one, and much more salutary than reading someone else's statistics. Extrapolation of results, because of comparable surgical mortality rates, into the statistical salvage rates of leading clinical centers where serious study of the disease is carried out, is surgical wishful thinking.

It is the author's belief that we are overdue for an audit of the surgical care of the cancer patient. When one considers the vastly improved situation resulting from the work of the maternal mortality committees in various American cities, directed toward a physiologic process whose mortality is minimal, one wonders at the laxity of our approach to a disease whose uninterrupted natural history is 100 per cent fatal.

The American College of Surgeons has taken a further step in the direction of "cancer control" by approving the recommendations of its Committee on Cancer, which go into effect in January 1956. Under the chairmanship of the late Dr. Edwin P. Lehman, the current cancer program of the College was reviewed and revised to maintain evolutional

continuity with present day hospital and surgical potential, rather than the status quo. Essentially there are only two changes in this revised program. The previous minimum standards recognized cancer diagnostic clinics, and cancer clinics. This concept has been altered to a more realistic definition, namely, that most of the approved clinics are actually cancer consultation services, and are now so named. Secondly, and of much more fundamental importance, the cancer registry has been made the basis of all hospital cancer programs. This simply means that the basic requirement of a hospital attempting to give any more than lip service to a cancer program necessitates the compilation of a continual and current boxscore of its cancer innings and winnings. This living record should be brought to the attention of the hospital staff at regular intervals, at least once yearly, so that the staff is made aware of its rate of successes and failures in treating cancer. This procedure allows comparison with documented results from other institutions, and would be a source of satisfaction if the comparison is favorable, and a spur to more serious effort if otherwise. Such an activity would appear to be the most innocuous approach to battening the cancer escape hatches, and the author heartily recommends the cooperation of all hospitals and their staffs in this new cancer program of the American College of Surgeons.

DANELY P. SLAUGHTER.

THE SURGEON AT WORK

TIBIOCALCANEAL FUSION: A SURGICAL TECHNIQUE

RAYMOND G. GIBERSON, M.D., and JOSEPH M. JANES, M.D., F.A.C.S.,
Rochester, Minnesota

MALUNION, accompanied by traumatic arthritis with serious dysfunction and disability, may at times be a sequel to fractures and fracture-dislocations of the astragalus. It is well accepted that a stiff, painless ankle and subastragalar joint are more serviceable than joints that exhibit limited painful motion.

When it is necessary to fuse both the astragalotibial and subastragalar joints, we have found the following method to be most valuable. The tibia, astragalus, and calcaneus are fused by bridging them with a tibial bone graft, which is held in position by fixation with screws. A transfibular approach is used.

Similar techniques have been described by Adams and by Marquardt; these authors advocated use of the distal portion of the fibula as a graft. A series of cases of "aviator's astragalus," in which this method of arthrodesis was used in some cases, has been presented recently by Coltart. One of us (Janes) first became acquainted with this procedure while serving in the Royal Air Force during World War II.[1]

INDICATIONS

Experience has shown that fusion of the damaged joints is required when extensive traumatic arthritis and deformity of the ankle and subastragalar joints are present.

The joints fused by this technique are the astragalotibial and the subastragalar. The method can be used whenever a fusion of these joints is indicated. We have found it most useful in repair of the ankle after fracture or fracture-dislocation of the astragalus. The results are superior to those following astragalectomy.

When comminution of bone is present or when the surfaces of the joint are involved in a fracture of the astragalus, it is often best to perform primary arthrodesis; in such cases, we have found this method extremely satisfactory. In a patient who had a painful pseudarthrosis between the tibia and calcaneus after removal of a fractured astragalus, arthrodesis was accomplished satisfactorily by use of this technique.

When panarthrodesis is required, it can be accomplished through the transfibular approach; the astragalotibial and the astragalocalcaneal joints are fused by means of a bridging tibial graft. The astragaloscaphoid and calcaneocuboid joints can be bridged similarly by small inlay grafts from the tibia.

TECHNIQUE

The procedure is carried out with the patient under general anesthesia. The skin is prepared with soap, water, ether, alcohol, and sodium ethylmercurithiosalicylate (merthiolate). A sterile stockinet is then rolled over the foot so as to cover the foot, leg, and thigh to the groin. Gum mastic is applied over the region where the incisions are to be made, to hold the stockinet firmly in place. The limb is then exsanguinated by application of an Esmarch bandage; a second Esmarch bandage is then applied as a tourniquet around the thigh, after which the first bandage is removed.

An incision is made through the stockinet and skin over the anteromedial surface of the tibia midway between the two palpable borders; a graft 6 inches (15.2 cm.) in length and ¾ inch (1.9 cm.) in width is outlined on the bone by means of a motor saw. The distal end of the graft is tapered and, while the graft is still in place, the required number of holes are drilled and countersunk (Fig. 1a). The number and position of the holes depend on the relative position of the tibia, astragalus, and calcaneus. The graft is then removed.

A long J-shaped incision is made over the lateral aspect of the leg, ankle, and foot. It overlies the fibula in its distal third and curves forward on the foot just posterior and inferior to the lateral

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[1]The method was learned from Air Commodore H. Osmond-Clark, F.R.C.S.

Fig. 1.

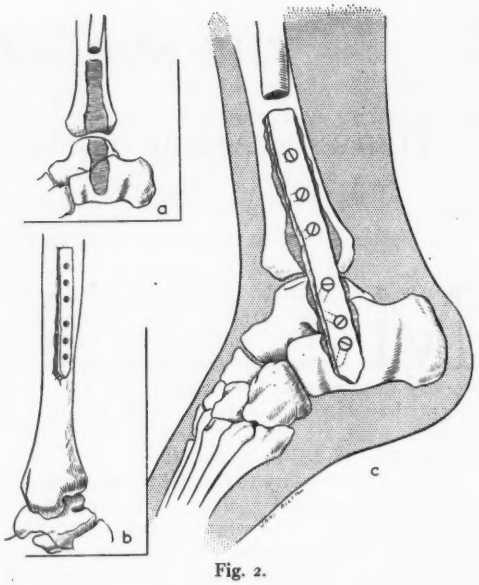


Fig. 2.

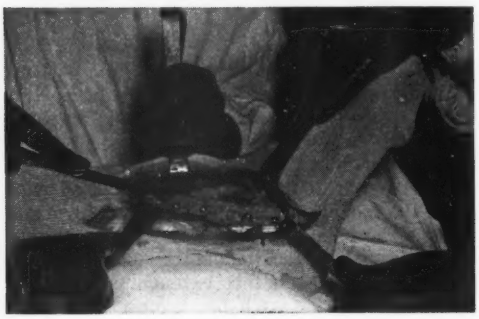


Fig. 3.

Fig. 4.

Fig. 1. a, Tibial graft cut and drilled prior to removal. b, Incision for transfibular approach.

Fig. 2. a, Bed fashioned in preparation for graft. b, Tibial graft. c, Tibial graft applied.

Fig. 3. The distal portion of the fibula has been removed and the tibial graft is in position; screws have been inserted for fixation.

Fig. 4. Plaster-of-paris cast applied at completion of operation; note strip of cast removed from lower anterior aspect.

malleolus (Fig. 1b). Through this incision, the distal portion of the fibula is removed, which usually involves resection of approximately 3½ inches (about 9 cm.) of the fibula. The cartilage is removed from the surfaces of the joint to be fused and the bones are aligned in their proper position. In some earlier cases we did not remove the cartilage. Chips of bone from the resected portion of the fibula are placed as indicated and the remainder usually is donated to the bone bank.

The lateral aspect of the tibia is made smooth and flat. A mortise is fashioned in the astragalus and os calcis (Fig. 2a) to receive the tibial graft (Fig. 2b). The graft is placed and holes are drilled in the tibia, astragalus, and calcaneus. Screws are then applied to hold the graft firmly in place (Figs. 2c and 3). Usually 3 screws in the tibia, 1 or 2 in the astragalus, and 1 in the calcaneus are sufficient. Chips of bone are applied about the graft as required. The incision is closed in layers.

Dressings are applied to the wounds and a plaster-of-paris cast is applied from the base of the toes to the upper third of the thigh. The foot is placed in the position of equinus at an angle of

about 10 degrees in males and 15 degrees in females. The knee is flexed slightly. A strip of plaster about 1 inch (2.5 cm.) in width is then removed from the anterior aspect of the cast extending from just below the knee to within 2 inches (about 5 cm.) of its lower end (Fig. 4). The tourniquet is removed from the thigh after the cast has been applied below the knee.

REPORT OF CASE

A 26 year old man was admitted to the hospital on June 11, 1951, because of a fracture of the left astragalus. He had sustained the fracture in a fall from a height of 25 feet (about 7.5 meters), when a hydroelectric pole which he had climbed broke at its base, falling to the ground and carrying the patient with it.

On admission, minimal swelling and deformity of the ankle were present. Roentgenograms at that time showed tibiofibular separation, as well as longitudinal splitting of the astragalus with separation of fragments (Fig. 5a and b).

A compression dressing was applied and the patient was placed in bed. On June 15, 1951, tibiocalcaneal fusion was carried out according to the technique just described. Postoperative roentgenograms showed the graft to be in proper position.

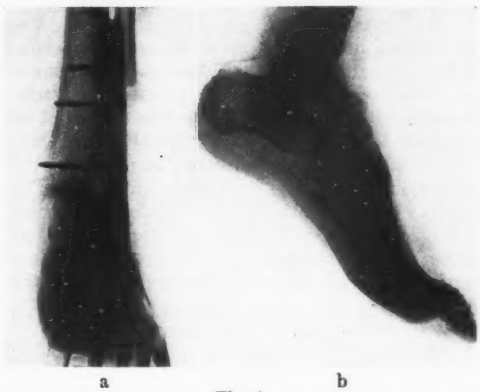
A new cast was applied and he was dismissed from the hospital on June 29, 1951. He was on crutches but was not bearing weight. Roentgenograms taken on September 19, 1951, showed the graft to be in good position and fusion to be taking place. The cast was removed at this time and a long leg cast was applied, in which a rubber heel was incorporated; he began to bear weight in 48 hours. He was walking without pain a week later.

The cast was removed October 10, 1951, and a leg brace was fitted. A roentgenogram made October 15, 1951, showed that firm union had taken place. He discarded the brace on January 16, 1952, and began doing light work.

When last seen, on June 25, 1952, he had sound tibiocalcaneal fusion, observed both clinically and in roentgenograms (Fig. 6a and b). He had no pain in his ankle or foot and he was back at his job of climbing poles. Considerable motion had developed in the midfoot, but he walked with a slight limp.

a b

Fig. 5.



a b

Fig. 6.

Fig. 5. a and b, Fracture on admission. Note split in astragalus, with separation of fragments; diastasis is present at the tibiofibular joint.

Fig. 6. a and b, Same ankle 1 year after tibiocalcaneal fusion.

COMMENT

We have used this method of arthrodesis for the treatment of 12 other patients. The transfibular approach has many advantages, although it has not been used widely since it was advocated by Goldthwait, in 1908. The exposure is excellent. We prefer to use a tibial bone graft rather than the excised portion of the fibula because of the greater strength and more suitable contour of the former.

Fixation by means of screws holds the parts firmly until fusion is complete. Movement of the ankle must be prevented by use of a cast for a period of 4 to 6 months.

Important details in the success of the operation are: (1) careful selection of patients; (2) complete removal of cartilage from the surfaces to be fused; (3) correction of deformity by removal of sufficient bone and the application of chips of bone; (4) accurate apposition of denuded surfaces; and (5) firm fixation until fusion is complete.

SUMMARY

A method of arthrodesis of the astragalotibiocalcaneal joints by a transfibular approach is described in detail. The distal portion of the fibula is resected and a tibial graft is applied, bridging the tibia, astragalus, and calcaneus. The graft is held in place by fixation by means of screws. This technique has proved satisfactory in a num-

ber of cases, as exemplified in a report of 1 of these cases.

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A METHOD OF REPAIR OF POSTPARTAL LACERATIONS OF THE CERVIX UTERI

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THE repair of postpartal lacerations or of Dührssen's incisions of the cervix uteri demands speed of execution, an even distribution of tension along the suture line, hemostasis, a minimal amount of interference with the normal blood supply, and the avoidance of pockets leading to fistulous tracts. The integrity of the external os also must not be impaired and the resultant scar along the mucosa should be smooth in order to minimize the formation of adhesions with the vaginal wall. The results obtained with the methods of repair now in vogue are generally quite satisfactory, but at times leave something to be desired. These methods depend upon (1) interrupted through and through sutures, (2) interrupted mattress stitches, (3) figure-of-eight sutures, or (4) various types of continuous sutures such as the interlocked or the Lembert.

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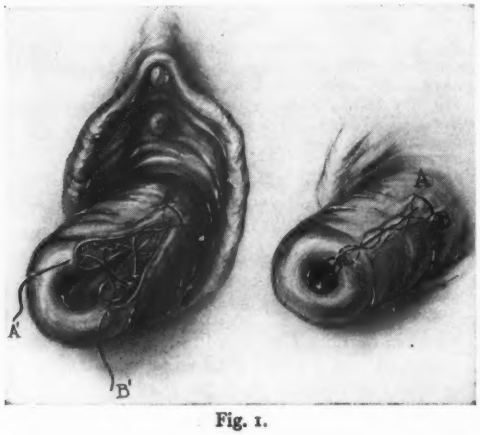


Fig. 1.

I should like to suggest a simple procedure for the repair of cervical lacerations which seems to fulfill the required conditions in a more effective manner than the current methods. The principles involved are similar to those described by Pettit[1] for the closure of transverse incisions of the lower abdomen. (1) The cervix is drawn down with sponge forceps for exposure. (2) The cut edges are carefully sponged free of blood clots. (3) A suture with a half length of chromic catgut (No. 0 or 1) is begun slightly above the upper limit of the laceration and continued uninterrupted down to the external os. Each bite extends half an inch into the torn muscle, and care is taken not to pierce the mucosa of either the cervical canal or the vagina. In the accompanying illustration (Fig. 1) it is seen to extend from point A to A'. (4) The needle is then unthreaded, the end left free, and the second half of the catgut is run in the same manner on opposite sides from point B to B'. (5) Gentle traction on the two ends at A' and B' bring the torn surfaces into even apposition under uniform tension. (6) A knot is tied at the external os and is the only one employed.

In the presence of excessive bleeding a single catgut stitch first may be inserted just above the upper angle of the tear, and individual bleeders may be ligated separately. However, in my hands they have been unnecessary as the suture here described has proved remarkably efficient in the control of any bleeding.

[1]Pettit, A. V. A method of wound closure in transverse abdominal incisions. West. J. Surg., 1943, 51: 479.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE volume, *Results of Research in Tuberculosis*[1] is written in German by several authors and represents a fine contribution to the literature on the fundamentals of tuberculosis.

The chapter by Uehlinger dealing with the pathologic anatomy of primary infection is particularly good and rather exhaustive considering the size of the volume (528 pages) with numerous well chosen histologic and roentgenographic illustrations. Late primary tuberculous infection is admirably discussed. The significance of this problem, clinically and pathologically, is stressed since improved social and economic conditions lead to a marked decrease in the occurrence of tuberculous primary complex during childhood. The question arises, will the acquisition of tuberculous primary infection in the adult change the course of the disease? This problem has frequently been discussed in the American literature by various investigators (Medlar, Sweany, and Terplan). The chapter on extra pulmonary primary complex by Beitzke emphasizes the importance of adhering to strict morphologic criteria of tuberculous primary complex. The diagnosis of tuberculous primary complex (e.g., in the tonsils, adenoids, larynx, and skin) should be accepted only if a tuberculous exudative caseous lesion is found in the organ itself with corresponding involvement of the regional lymph nodes. In an interesting and challenging chapter on "Sepsis Tuberculosa Gravissima" (Severe Tuberculous Sepsis) Beitzke attempts to draw a sharp border line between this entity and that of typhobacillose Landouzy. He points out that typhobacillose may heal completely while acute tuberculous sepsis has an absolutely bad prognosis. Many American physicians interested in tuberculosis, perhaps because of the influence of Rich and Feldman, are prone to reject the existence of this entity.

Beitzke discusses the incidence of avian tuberculosis in humans in one chapter and concludes that it is not so rare as has been supposed. In the chapter on the pathologic anatomy of tuberculosis in post war Germany, Giese points out that hunger and emaciation abolish the ability of the individual host to localize the tuberculous infection. Burkhardt has written an interesting account of the relationship of diabetes and tuberculosis. This combination occurs largely in the middle and older age group. He believes this combination is not as frequent as assumed. The evidence he presents indicates that caseous tuberculosis occurs more frequently in diabetic patients than in nondiabetics. Hematogenous dissemination, on the other hand, occurs less frequently in diabetics than in nondiabetics. The management of tuberculosis with pneumoperitoneum is dealt with in some detail by Nagel. Many workers in this country will agree with his conclusions that pneumoperitoneum has an important place in the therapy of pulmonary tuberculosis. Others would definitely disagree. Wernli-Haessig has an admirable discussion on the healing of pulmonary tuberculosis and deals with the prognosis of the different types from the standpoint of medical and social criteria. There is a short chapter by St. Engel on the management of tuberculosis among children which deals chiefly with general hygienic measures such as proper diet, rest, fresh air, and so forth. In the United States there is a growing conviction that chemotherapy is an essential part of the management of many such cases, particularly those which do not respond rather promptly to general hygienic measures. Other chapters which will interest the reader are the one dealing with tuberculosis of the mouth by Kranz and another on the effects of alcohol and tobacco on tuberculosis by Rickmann.

The book is beautifully bound and printed with easily read type. The illustrations are excellent and well selected. The bibliography following each chapter is very extensive and taken predominantly from the German literature. It is recommended to all physicians who are interested in tuberculosis.

KARL H. PFUETZE.

IN the third volume of *Clinical Orthopaedics*,[2] edited by Dr. Anthony F. DePalma, Section 1 is devoted to "Soft Tissue Conditions Around Joints," and Section 2 to "General Orthopaedics." This volume has been carefully evaluated and compared to Numbers 1 and 2. In order to determine the place of this number, the Preface of Volume 1 has been reviewed. The Preface indicates: (1) "the need for additional outlets in the literature for material of orthopaedic interest," (2) that "the findings of valuable investigations are published in journals conceived primarily for general surgery; hence they are lost to those truly interested in them"; (3) that "avenues of expression

[1] ERGEBNISSE DER GESAMTEN TUBERKULOSEFORSCHUNG. Edited by H. Beitzke, St. Engel, L. Heilmeyer, and J. Hein. Vol. 2. 528 pages, illustrated. Stuttgart: Georg Thieme, 1953.

[2] CLINICAL ORTHOPAEDICS; No. 3. SOFT-TISSUE CONDITIONS AROUND JOINTS. Anthony F. DePalma, M.D., Editor-in-Chief. With the Assistance of the Associate Editors and the Board of Advisory Editors. 230 pages, illustrated. $7.50. Philadelphia, London, Montreal: J. B. Lippincott Co., 1954.

for the ever-increasing subdivisions of orthopaedic surgery and allied specialties" are needed; (4) that "the orthopaedic group as a whole should have a medium in which to keep the general practitioner and the surgeon in allied fields abreast of the rapidly growing scope of orthopaedic surgery." The material disseminated should be of scientific, practical, and academic value to the aforementioned groups.

Section 1 of Number 3 is entitled "A Symposium on Soft Tissue Conditions Around Joints." While the 15 articles are individually well written, unfortunately they are not combined into a unit. There are 7 articles dealing directly with the knee joint, 3 of which relate only to the semilunar cartilage and 3 to various types of dislocation of the patella. The individual articles could possibly be better correlated to avoid repetition and to define more clearly differences of opinion. Many conditions coming to the attention of the general practitioner or surgeon are not mentioned or only briefly so, e.g., acromioclavicular separation, tennis elbow, and torn quadriceps tendon. In the paper on "Injuries of the Medial Meniscus" the author says that "additional diagnostic information is gained through eight signs, seven by the author and one by McMurray." It might be recalled that some of these physical signs are listed in the section on "Lesions of Semilunar Cartilages" in Willis Campbell's textbook of orthopedic surgery published in 1930.

In the section on "General Orthopaedics" a method of knee fusion reporting 3 operative cases is presented. Dr. Leslie V. Rush's article on "Closed Medullary Pinning of Colles' Fracture" is an interesting and provocative report of 50 consecutive cases. A paper by Dr. H. Kelikian on "Vascular Relations of the Ankle and Their Clinical Significance" is included.

The question arises whether the goal of *Clinical Orthopaedics* is not too broad. It is admittedly difficult to prepare symposia that will at once be of helpful service to general practitioners, surgeons, and orthopedic surgeons. KENATH H. SPONSEL.

IN this period of rapid development in the field of chemotherapy, there exists a definite need of a concise, usable monograph on the management of patients with surgical infections. Colonel Pulaski has served this need by the publication of the volume entitled *Surgical Infections*,[1] which indicates the relative importance of antibiotic therapy and operative procedures in the prevention or control of surgical infections.

The book is relatively short and is adaptable for use as a manual for students, interns, residents, or clinicians who will be dealing with the prophylaxis or treatment of surgical infections.

The first part of this monograph deals with the antibiotic agents themselves and their relation to infection in general. Included in this portion is information concerning these drugs which will be of value to investigators as well as clinicians. The principles of early, accurate, and complete diagnosis and the administration of properly selected antibiotics in adequate dosage are emphasized as adjuncts to timely surgical intervention. The very clear discussion of the proper use of these agents as aids to surgical treatment reflects Colonel Pulaski's broad clinical and experimental experience in this field.

The second portion of the book will serve as a guide to the practicing clinical surgeon. It includes discussions on the use of chemotherapeutic agents for the prevention or treatment of specific surgical infections and regional infections in wounds. The method of selecting the proper antibiotic agent for each lesion, the dosage, and the most efficient route of administration are indicated. Emphasis is placed upon the limitations of these agents and the potential harm which may result from their improper use. Colonel Pulaski reiterates the principle that chemotherapy should not be used as a substitute for competent surgical care.

Because of the rapid progress made in this field during the past year, data on tetracycline unfortunately is not included.

The monograph is efficiently indexed. References are complete and current, and the figures and tables are easily understood. W. A. ALTEMEIER.

A MUCH needed book entitled *The Hepatic Circulation and Portal Hypertension*[2] well summarizes our present knowledge of normal and abnormal circulation of the liver. Dr. Child has assembled this prolific material as basic discussions of anatomy, circulatory physiology, regeneration, abnormal states such as the relation of vascular changes to ascites, shock, hemorrhage, etc., and concluded with the evaluation of abnormal case problems and rationale of surgical therapy. It is presented in a concise, readable fashion with clarity.

We are indebted to his excellent correlation of the basic science information on the subject, yet his own interests are in the study of the clinical problem. By evaluating experimental procedures on monkeys with the portal venogram in addition to the usual analysis of the results, he has acquired the assurance to proceed with such unusual operations on humans as the two stage removal of the pancreas and the portal vein. Venography at surgery is highly recommended to aid in effective surgical management. He has not found the end-to-side portacaval procedure to be detrimental to liver function and he only presents the arguments of others about the efficacy of hepatic artery ligation. No evidence for significant arteriovenous shunting in cirrhosis is presented.

The reader is wisely stimulated by Dr. Child that the problem is near its climax. The tools for study

[1] SURGICAL INFECTIONS. PROPHYLAXIS—TREATMENT—ANTIBIOTIC THERAPY. By Edwin J. Pulaski, M.D., D.M.Sc. (Surgery). 332 pages, 101 illustrations. $7.75. Springfield, Ill.: Charles C Thomas, 1954.

[2] THE HEPATIC CIRCULATION AND PORTAL HYPERTENSION. By Charles G. Child, III, M.D. 444 pages, 132 illustrations. Philadelphia and London: W. B. Saunders Co., 1954.

and management are at hand, and many significant truths are yet to come. One of these that is being debated is: why must portal decompression be done with cirrhosis and yet complete ligation of the portal vein without cirrhosis need no decompression.

DONALD C. BALFOUR, JR.

A GENERAL survey of neurologic surgery in infants and children is presented in *Neurosurgery of Infancy and Childhood*.[1] The authors lay particular stress on the varied disciplines peculiar to the examination and management of patients in this age group. While they note that the book is not intended to be "an encyclopedic text of reference" for the field of neurosurgery in childhood, it would seem that it lacks little of achieving this distinction.

The book is exceptionally well organized with logical divisions considering congenital anomalies, hydrocephalus, trauma, tumors, infections, vascular disorders, epilepsy, and, appropriate even for this enlightened age, encephalopathy due to lead. The chapter headings under these divisions take up sequentially the various entities with details of examination methods applicable to the particular condition, followed by delineation of treatment methods which have been found most satisfactory to date in the experience of the authors and their co-workers at the Children's Medical Center in Boston. No detailed case reports are given, but in almost all instances photographic examples of cases representative of the condition described in the text and illustrations of the x-ray, electroencephalogram, and operative findings and techniques are appropriately placed.

The illustrations from a technical and an artistic standpoint are excellent examples of clinical medical photography and medical illustration. A fairly extensive bibliography and a thorough index add appreciably to the usefulness of the book.

This book could well be read by every physician who has any interest in the care and handling of infants and children: if only that they may gain proper appreciation of what can be accomplished by neurosurgical means to alleviate the suffering of some of these unfortunate individuals, and to correct the deformities of others.

HALE HAVEN.

THE monograph containing 149 pages of text entitled *The Billroth I Gastric Resection; with Particular Reference to the Surgery of Peptic Ulcer*[2] is a nicely bound volume printed in an excellent fashion on good paper. The illustrations are clear and numerous. Particularly fine are the line drawings which are used to illustrate some of the technical procedures.

The first of 8 chapters contains a brief history of gastric resection which is well compiled and is a good reference work for the student of this subject. Successive chapters concern the rationale of subtotal gastric resection for peptic ulcer, selection of patients for subtotal gastric resection, and preoperative care. A chapter is devoted to surgical technique of the Billroth I resection. The author's method of handling the more serious technical problems in gastric surgery are fully described. The author's routine of postoperative care and the care of the complications form another chapter. The postgastrectomy syndrome, theories as to its cause and prevention are discussed. The final chapter summarizes the criticisms and advantages of the Billroth I gastric resection. The authors are obviously enthusiastic about the Billroth I gastric resection and have documented their preference for this type of surgical procedure in a thorough manner.

Following the text there are short biographic sketches of some of the more prominent contributors to the knowledge of gastric surgery since the time of Billroth. These are interestingly written and are helpful for the student first taking the subject of gastric surgery. There is an extensive bibliography followed by an adequate index which is listed by subject matter and by author.

The reviewer has read this monograph with pleasure and profit. The volume should be in the hands of every surgeon who is interested in gastric surgery.

THOMAS C. DOUGLASS.

THE 1954 edition of *Current Therapy*,[3] the sixth of an annual series, continues to provide current methods of treatment in a quick, adequate reference volume for the busy physician. It contains information concerning treatment with new drugs and methods, as well as long tested therapeutic agents. This revision presents the re-evaluation of therapy and elaboration of the knowledge gained since publication of the previous editions. Twelve consulting editors together with 377 contributors, of whom 192 are new this year, provide the information in this book. It is well edited, and the print is clear and easy to read. It has a complete index of subjects, authors, and a useful roster of drugs in addition to conversion tables for weight systems and percentage solutions.

The subject matter includes a discussion of diseases of infectious nature and of systems as well as those due to physical or chemical agents, disorders of metabolism or nutrition, and obstetric or gynecologic conditions. The reviewer has found the discussions to be brief, concise, specific, and quite inclusive considering that the editor was forced to cover such a large subject in 850 pages. Multiple methods of therapy are given for certain subjects, as in the discussion of the purpuric states, peptic ulcer, myocar-

[1] NEUROSURGERY OF INFANCY AND CHILDHOOD. By Franc D. Ingraham, M.D., and Donald D. Matson, M.D. 456 pages, 381 illustrations. Springfield, Ill.: Charles C Thomas, 1954.

[2] THE BILLROTH I GASTRIC RESECTION; WITH PARTICULAR REFERENCE TO THE SURGERY OF PEPTIC ULCER. By Horace G. Moore, Jr., M.D., and Henry N. Harkins, M.D., Ph.D., F.A.C.S. 175 pages, 36 illustrations. $7.50. Boston: Little, Brown & Co., 1954.

[3] CURRENT THERAPY 1954; LATEST APPROVED METHODS OF TREATMENT FOR THE PRACTICING PHYSICIAN. Edited by Howard F. Conn, M.D. 808 pages. $11.00. Philadelphia and London: W. B. Saunders Co., 1954.

dial infarction, hemophilia, and regional ileitis to mention specific examples. This should add to the value of the book. Rheumatoid arthritis is covered in 10 pages beginning with an adequate discussion of the therapeutic approach, followed by methods of therapy which include a comprehensive discussion of the use of gold salts, ACTH, cortisone, and hydrocortisone. The advantages and pitfalls are stressed in each form of therapy outlined. The use and misuse of parenteral fluids are covered extremely well within 14 pages.

One must conclude that this volume should prove to be most useful and helpful for the physician in general practice. It is an excellent review of present day therapy presented by authors from all sections of this country and is highly recommended.

GEORGE C. TURNBULL.

AN excellent monograph *Diseases of the Liver*[1] by Mitchell A. Spellberg is designed specifically for the medical clinician. A foreword by Walter L. Palmer of the Department of Medicine, University of Chicago indicates that the author has employed three approaches to the evaluation of hepatic disease—clinical observations; anatomical studies obtained by needle or operative biopsy; and physiologic investigations through so-called liver function tests.

In the preface, Dr. Spellberg states that the book is written from the viewpoint of a clinician primarily for clinicians, and in this the author has certainly succeeded. Although there are no separate sections on physiology or anatomy, these aspects are considered in discussions on abnormal hepatic behavior. Special emphasis has been placed on diagnosis, and the author has attempted to correlate etiologic factors with anatomic alterations and physiologic aberrations in presenting the clinical picture.

Each clinical entity is discussed in the classic sequence used by many authors as follows: definition of the subject to be described, its morbid anatomy, abnormal physiology, etiology, symptoms, signs, diagnosis, and treatment. The book is divided into 12 sections on following subjects: clinical laboratory tests as a mirror of hepatic function, morphologic approach to the diagnosis of liver disease, differential diagnosis of jaundice, neoplasms and cysts of the liver, response of the liver to chemical toxins (toxic hepatitis), effects of infectious agents on the liver, role of diet in liver disease, anatomy of the liver and its vascular supply—disease of the liver resulting from disturbances in the major vessels, cirrhosis; role of the endocrine glands in diseases of the liver—hepatorenal relationship, liver in various diseases, and disease of the liver associated with inborn errors of metabolism.

Some features of the book will be welcomed by the busy clinician. In section 1 the principal functions of the liver are listed and in a parallel column tests which are designed to determine the normalcy or abnormal physiology of these functions are indicated. Moreover, methods of performing the various tests are outlined and their relative importance in the diagnosis of disease is clearly delineated. At the conclusion of this section a table of the more reliable liver tests sets forth values and alterations in various disease states. The contents of each section are summarized in boldfaced type at the end of every chapter. This is a brief and accurate condensation so that at a moment's glance the pertinent information contained in the section can be easily ascertained. Summaries also appear at the conclusion of the various subjects within a section. For example, the causes of jaundice and its differential diagnosis is well covered and in addition each variety is summarized. Illustrations are not plentiful, but they are for the most part well chosen and depict some important phases of hepatic disease.

At the conclusion of the book the author lists some 2,400 references to articles by physiologists, biochemists, experimenters, surgeons, and internists. These cover almost every angle of liver derangement and constitute a well selected bibliography.

The healthy as well as the morbid deportment of the liver is controversial and, therefore, there is a wholesome difference of opinion concerning many phases of hepatic abnormality. There must, therefore, also exist some disagreement as to the manner and degree to which the subject matter should be presented in a monograph for the clinician. For example, there is no discussion of the embryology of the liver and hence there is only a brief mention of congenital atresias of bile ducts under the general subject of obstructive biliary cirrhosis. Nothing has been said about traumatic injuries to the liver which may give rise to various maladies which otherwise might be overlooked or completely undiagnosed. Among these could be mentioned liver abscess, subphrenic abscess, subphrenic accumulation of bile, hemobilia, or hemocholia.

The etiology, pathology, and complications of cirrhosis are described extensively and the various opinions concerning its behavior are reviewed impartially and applied accurately to clinical use. There is no discussion as to the probable causes of jaundice during the course of portal cirrhosis although the author states that clinically detectable icterus may be present in 30 to 48.9 per cent of the cases and that persistent jaundice is of grave prognostic import. The accompaniment of portal cirrhosis with splenic enlargement is mentioned, however, its importance in prognosis is not discussed. One wonders whether an overfilling of this reservoir may not imply imminent vascular decompensation of the liver.

The subject of esophageal varices has been well handled and of course the control of this perplexing problem is not as yet solved. The author believes that the high pressure within the portal vein is of great importance in the causation of bleeding varices. However, varices do occur without portal hypertension and their presence does not necessarily presage bleeding; moreover, the height of the portal pressure is not an accurate indication of whether or not an esophageal varix will bleed. Undoubtedly there is a

[1] DISEASES OF THE LIVER. By Mitchell A. Spellberg, M.D., F.A.C.P. 646 pages, 92 illustrations. $16.50. New York: Grune & Stratton, Inc., 1954.

connection between portal hypertension and bleeding varices but the author correctly asserts that its exact nature is at present unknown. Another point which the author raises is the amount of blood which should be given in the presence of an exsanguinating hemorrhage. He maintains that restoration of blood volume should be very slow and that when the erythrocytes reach around 3 to 3½ million per cubic millimeter transfusions should be discontinued because of the danger of distending the varices and starting another hemorrhage. The relationship between the general systemic arterial blood pressure and pressure within the esophageal varix is not intimate and is only reflected when the arterial pressure reaches extremely low levels, although there certainly is a close parallel between the arterial and venous pressures in the esophagus. Many observers believe that it is better to restore the entire blood volume quickly and as completely as possible, so that if, and when another hemorrhage occurs the patient may not be reduced to dangerously low and prolonged shock levels in the presence of an already ischemic liver. The Trendelenburg position has been used in the treatment of esophageal hemorrhage for some time. The author assumes that the head down position provides for free access of blood to the hepatic and azygos veins and the vena cava. However, this position interferes with free respiration due to interference with diaphragmatic motion and adds to the anoxic anoxemia already present. For this reason many clinicians prefer the semirecumbent position which is also desired by most patients. It has been suggested by some surgeons that a phrenic crush on the left side may curtail the sucking action within the esophagus during inspiration, without interfering with the negative pressure in the right chest where free egress of hepatic venous blood into the vena cava is desirable.

On page 358 the author states that it is occasionally difficult "to bring the portal vein and vena cava together without undue tension. This obstacle has been surmounted by the use of a vitallium tube or vein graft to bridge the gap." A vitallium tube may lead to thrombosis at the site of anastomosis and, therefore, it is not used by most surgeons. This is true of any foreign body used to establish venovenous anastomosis although it is agreed that some surgeons have recommended it.

The reduction of blood sodium in spite of the reduced renal excretion is explainable on the basis of accumulation of the sodium salt in the ascitic fluid. However, it is now known that some sodium is stored in muscle and bone, and perhaps there is an abnormal storage in these tissues in the presence of portal cirrhosis. This subject needs further elucidation.

Diseases of the Liver is recommended to the internist who should know the indications, contraindications, and limitations of surgical treatment. It is also a valuable book for the surgeon who should be a good medical clinician equipped with the knowledge to know when, as well as the ability to know how, to perform surgical operations. J. K. BERMAN.

IN the *Atlas of Orthopedic Traction Procedures*[1] Dr. Scuderi has clearly portrayed many types of traction procedures applicable to the spine and extremities. It represents a total survey of this field and may be used for reference in considering specific traction treatment problems. The various types of skeletal and skin traction are clearly illustrated in photographs and diagrams. Under each type of traction there is a list of necessary equipment, the method of application, and the author's comment. The comments are directed to the advantages, disadvantages, and hazards of each setup. The author expresses his personal preferences and the reasons therefor.

Dr. Scuderi has ably accomplished his goal in producing a guide for traction procedures. The reviewer plans to have a copy placed in each of the hospitals in which he works. This is a strong recommendation for its acceptance as a standard reference in all general hospitals. Its use will guide physicians, surgeons, house officers, nurses, and technicians in efficient orthopedic care. KENATH H. SPONSEL.

[1]ATLAS OF ORTHOPEDIC TRACTION PROCEDURES. By Carlo Scuderi, B.S., M.D., M.S., Ph.D. 230 pages, 124 illustrations. $12.50. St. Louis: The C. V. Mosby Co., 1954.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

FLUID BALANCE IN SURGICAL PRACTICE. By L. P. Le Quesne, M.A., B.M., B.Ch. (Oxon), F.R.C.S. (Eng.). 130 pages, 41 illustrations. $3.50. Chicago: The Year Book Publishers, Inc., 1954.

BABCOCK'S PRINCIPLES AND PRACTICE OF SURGERY. Edited by Karl C. Jonas, B.S., M.D., M.S. (Surg.), F.A.C.S., F.I.C.S. 1543 pages, with 1006 illustrations and 10 colored plates. $18.00. Philadelphia: Lea & Febiger, 1954.

THE ANATOMY OF THE BRONCHIAL TREE; WITH SPECIAL REFERENCE TO THE SURGERY OF LUNG ABSCESS. 2nd ed. By R. C. Brock, M.S. (Lond.), F.R.C.S. (Eng.), F.A.C.S. 243 pages, 157 illustrations. $11.00. London, New York, Toronto: Geoffrey Cumberlege, Oxford University Press, 1954.

LOOK BETTER, FEEL BETTER. By Bess M. Mensendieck, M.D. Foreword by Paul B. Magnuson, M.D. 276 pages, illustrated. $3.50. New York: Harper & Brothers, 1954.

EL EMBARZO, EL PARTO Y EL RECIEN NACIDO; MANUAL PARA PARTERAS RURALES. By Leo Eloesser, Edith Galt, and Isabel Hemingway. 146 pages, 66 illustrations. $0.35. A teacher's guide for its use: GUÍA DE ENSEÑANZA. By Leo Eloesser. 47 pages, 3 illustrations. $0.10. México: D.F.: Instituto Indigenista Interamericano, 1954.

MEDICINA NUCLEARE; INTRODUZIONE ALLE APPLICAZIONI MEDICO-BIOLOGICHE DELLA FISICA NUCLEARE. By Aldo Perussia *et al.* 877 pages, 143 illustrations. Roma: Il Pensiero Scientifico Editore, 1954.

CANCER OF THE THYROID. By John deJ. Pemberton, M.D., and B. Marden Black, M.D. 47 pages, 16 illustrations. Free. New York: The American Cancer Society, Inc., 1954.

INTRODUCTION TO SURGERY. By Virginia Kneeland Frantz, M.D., and Harold Dortic Harvey, M.D. 3rd ed. 233 pages, 13 illustrations. $4.00. New York: Oxford University Press, 1954.

A PRACTICAL MANUAL OF DISEASES OF THE CHEST. By Maurice Davidson, M.A., M.D. (Oxon.), F.R.C.P. (Lond.), with the assistance of John H. Friend, M.D. (Lond.), M.R.C.P. (Lond.). 4th ed. 647 pages, 255 illustrations. $19.25. London, New York, Toronto: Geoffrey Cumberlege, Oxford University Press, 1954.

DISEASES OF THE SKIN; FOR PRACTITIONERS AND STUDENTS. By George Clinton Andrews, M.D., F.A.C.P. 4th ed. 877 pages, 777 illustrations. $13.00. Philadelphia and London: W. B. Saunders Co., 1954.

THE MECHANISM OF LABOUR. By Erik Rydberg, M.D. 180 pages, 38 illustrations. $4.75. Springfield, Ill.: Charles C Thomas, 1954.

RETROPUBIC PROSTATECTOMY; FOR BENIGN ENLARGEMENT OF THE PROSTATE GLAND. By Francis A. Beneventi, M.D., F.A.C.S. Art direction and 44 original drawings by William P. Didusch. 227 pages, 74 illustrations. $11.00. Springfield, Ill.: Charles C Thomas, 1954.

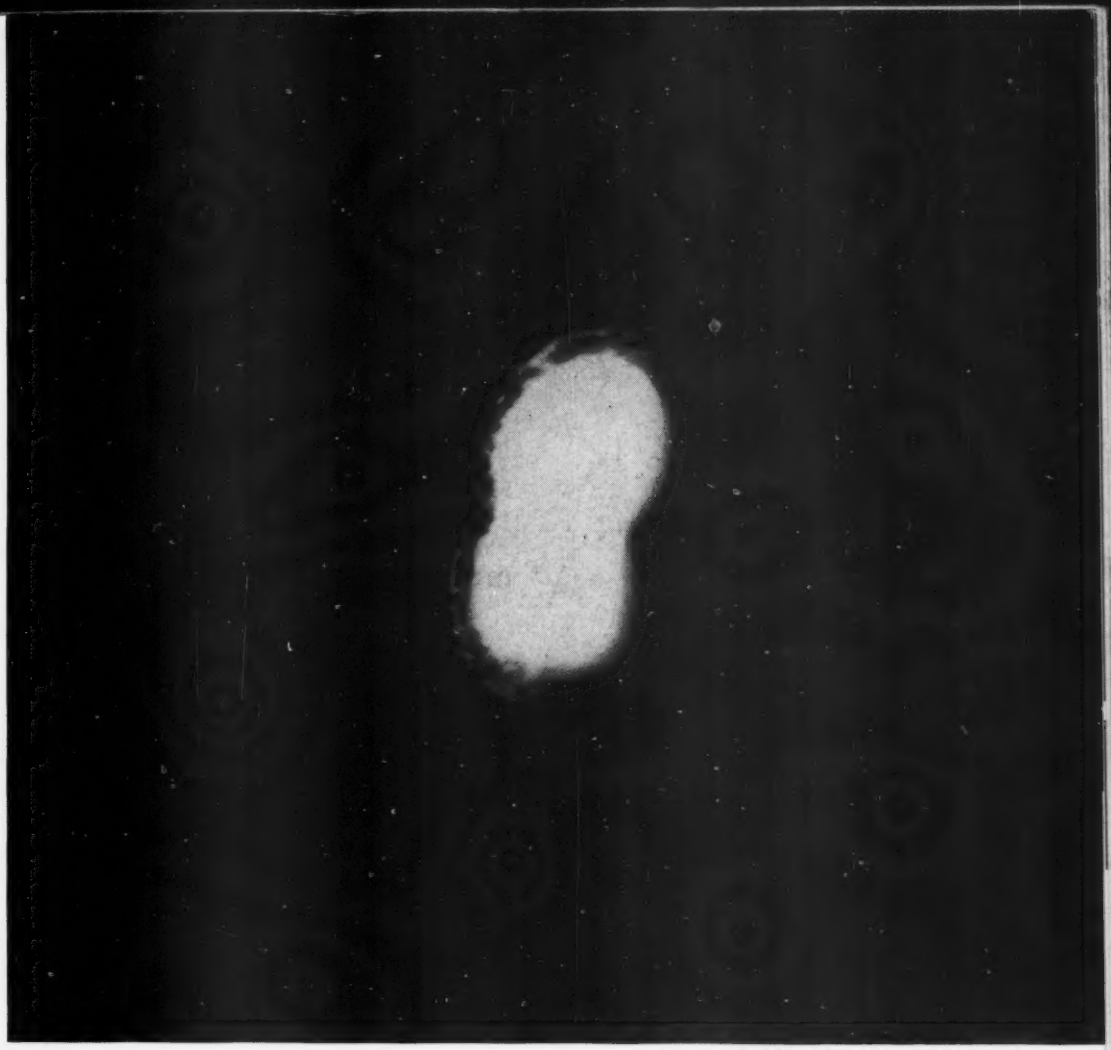
A HISTORY OF MEDICINE. By Ralph H. Major, M.D. Vols. 1 and 2. 1155 pages, illustrated. $14.50. Springfield, Ill.: Charles C Thomas, 1954.

SURGICAL TREATMENT OF CANCER OF THE CERVIX. Edited by Joe V. Meigs, M.D. 462 pages, illustrated. $12.00. New York, London: Grune & Stratton, 1954.

CORRESPONDENCE

THE PATHOGENESIS OF ASCITES AND A CONSIDERATION OF ITS TREATMENT—A CORRECTION

ATTENTION is called to a printer's error in sentence construction made in the article by John L. Madden and associates entitled "Pathogenesis of Ascites and a Consideration of Its Treatment" published in the October 1954 issue. This error appears on page 386 and is the last sentence in the first paragraph in the section "Method and Material." In the journal, this sentence reads: "In 10 of these, absent irreversible ascites was present clinically and in the other 4." This should have read: "In 10 of these irreversible ascites was present clinically and in the remaining 4 ascites was absent."



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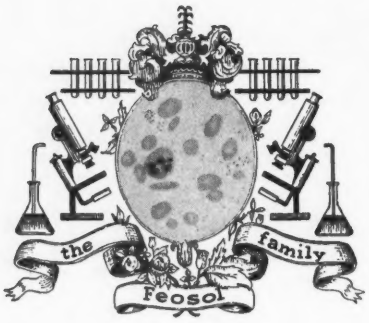

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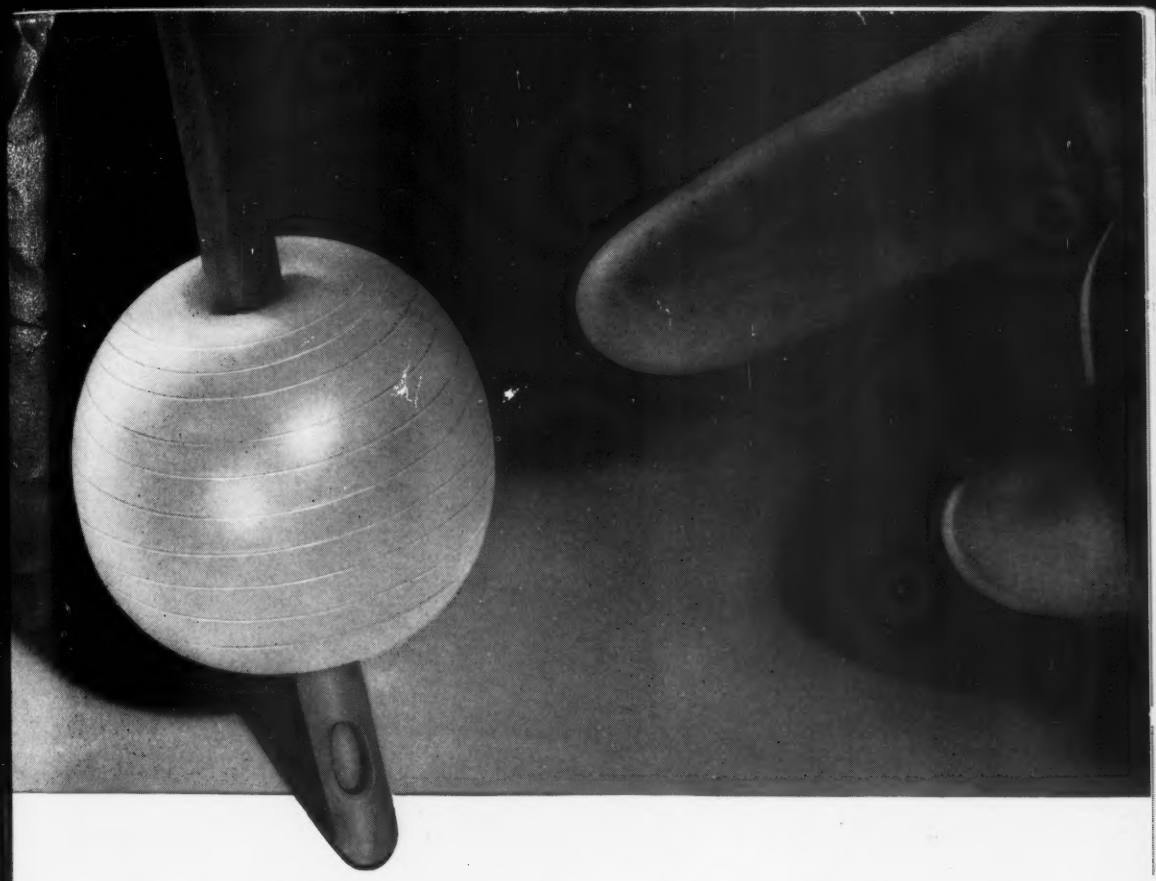

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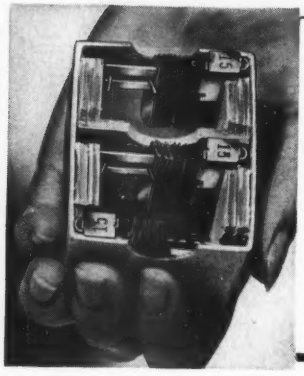

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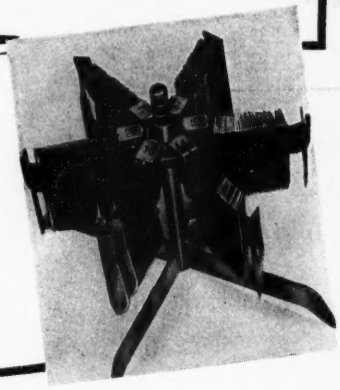

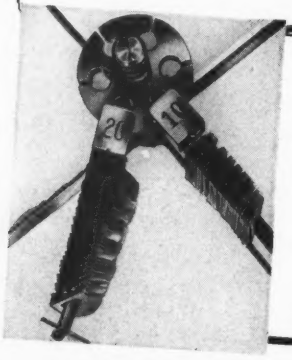

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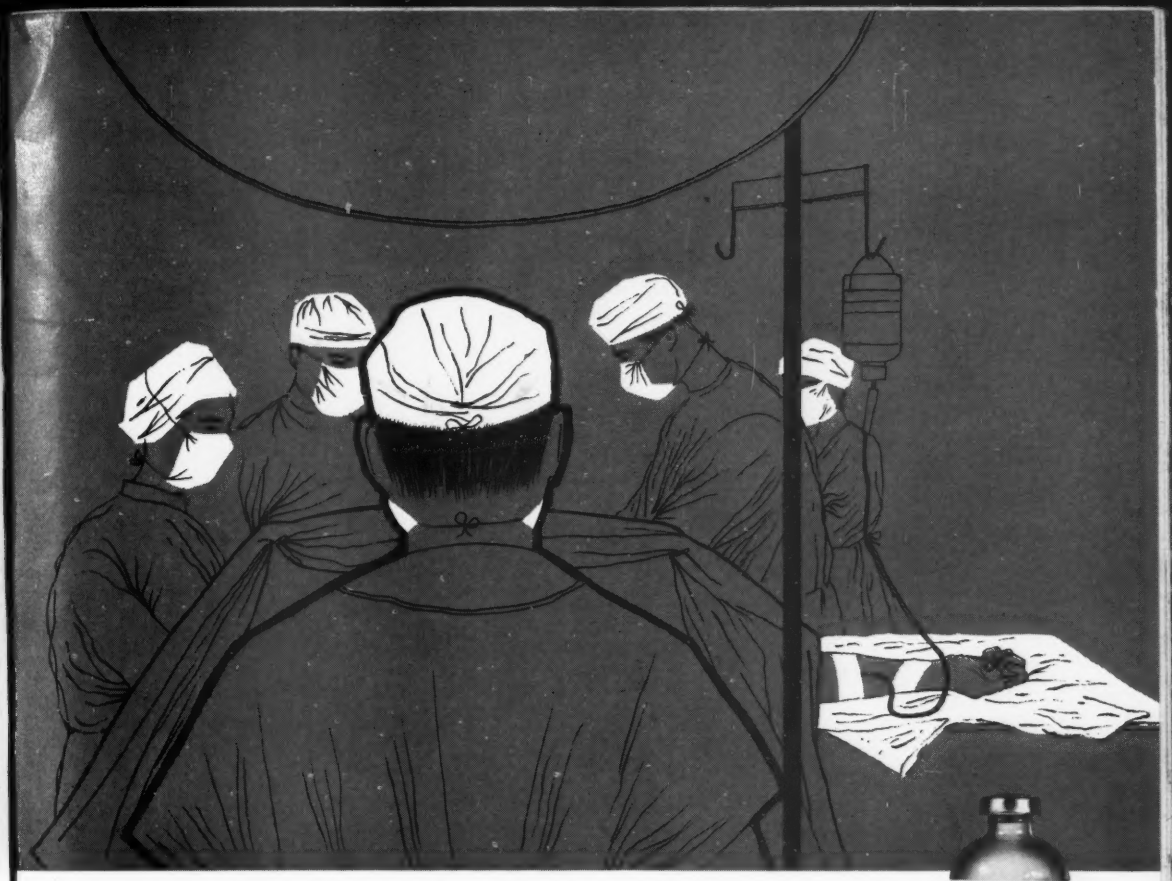

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1. Helrich, M.; Papper, E. M., & Rovenstine, E. A.: *Anesthesiology* 11:33, 1950. 2. Stephen, C. R., & Martin, R.: *North Carolina M. J.* 12:501, 1951. 3. Phillips, H. S.: *Anesth. & Analg.* 32:56, 1953.

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1. Goldsmith, G. A.: Application to Human Nutrition, in Bourne, G. H., and Kidder, G. W.: Biochemistry and Physiology of Nutrition, New York, Academic Press Inc., 1953, chap. 23, p. 505.
2. Recommended Dietary Allowances, Washington, D. C., National Academy of Sciences—National Research Council, Publication 302, 1953, p. 23.
3. Ekstein, H. C.: Fat in Nutrition, in Handbook of Nutrition, A Symposium, ed. 2, Philadelphia, The Blakiston Company, 1951, p. 23.
4. Sherman, H. C.: Chemistry of Food and Nutrition, ed. 8, New York, The Macmillan Company, 1952, (a) p. 30; (b) p. 198; (c) p. 115; (d) p. 103.
5. McLester, J. S., and Darby, W. J.: Nutrition and Diet in Health and Disease, ed. 6, Philadelphia, W. B. Saunders Company, 1952, pp. 130-135.
6. Smith, F. H.: The Use of High Fat Diets for Constipation, J.A.M.A. *88*:628 (Feb. 26) 1927.
7. Okey, R.: Cholesterol Content of Foods, J. Am. Dietet. A. *21*:341 (June) 1945.

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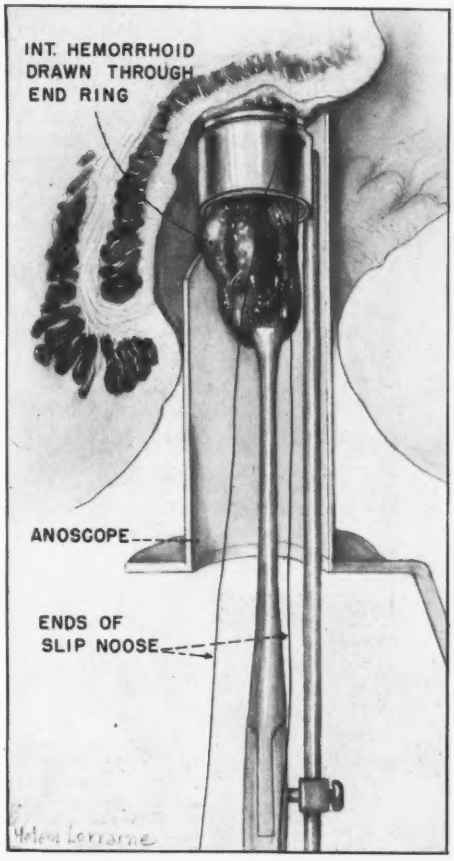

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No. 577B, medium, 5½" bar, 4" foot plate.
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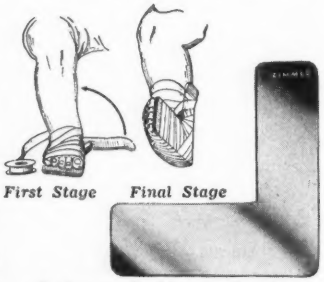
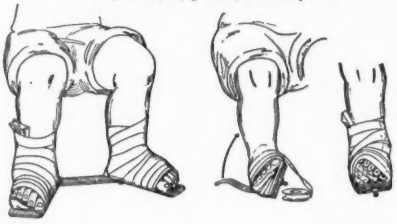
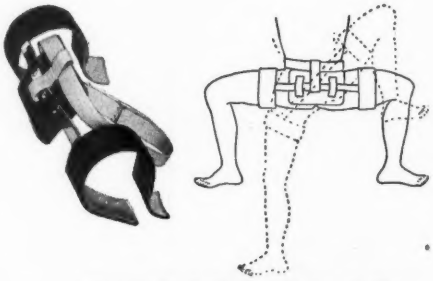


Valgus Talipes Splint

No. 578A, large, right or left, 5" foot plate.
No. 578B, medium, right or left, 4" foot plate.
No. 578C, small, right or left, 3" foot plate.
(In ordering, please specify whether right or left is required.)





Congenital-Dislocation-of-Hip Splint

No. 780A, large, adjustable frame, 13½" to 16¼" (outside measurements).
No. 780B, medium, adjustable frame, 11¾" to 13½".
No. 780C, small, adjustable frame, 9¼" to 11½".
Splint applied posteriorly with dotted lines showing range of movement permitted.

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+	
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Ascorbic Acid	150 mg.
Liver Fraction 2, N.F.	200 mg.
Thiamine Mononitrate	6 mg.
Riboflavin	6 mg.
Nicotinamide	30 mg.
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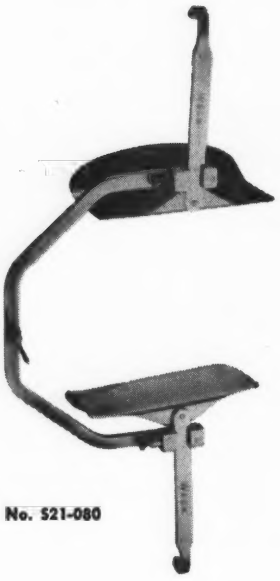

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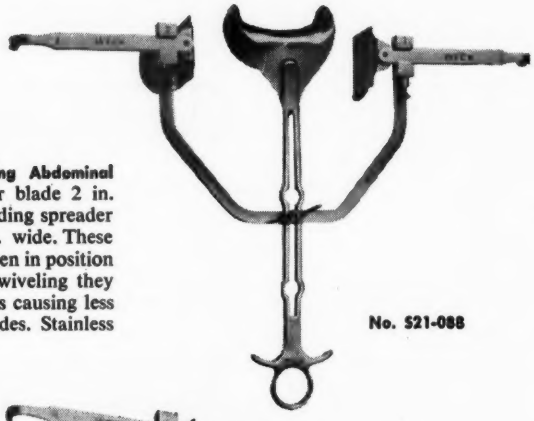

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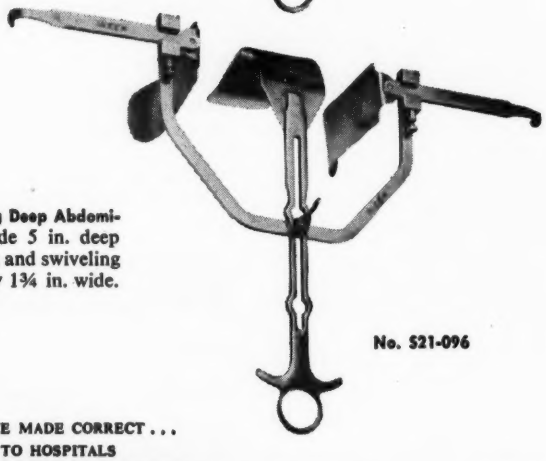

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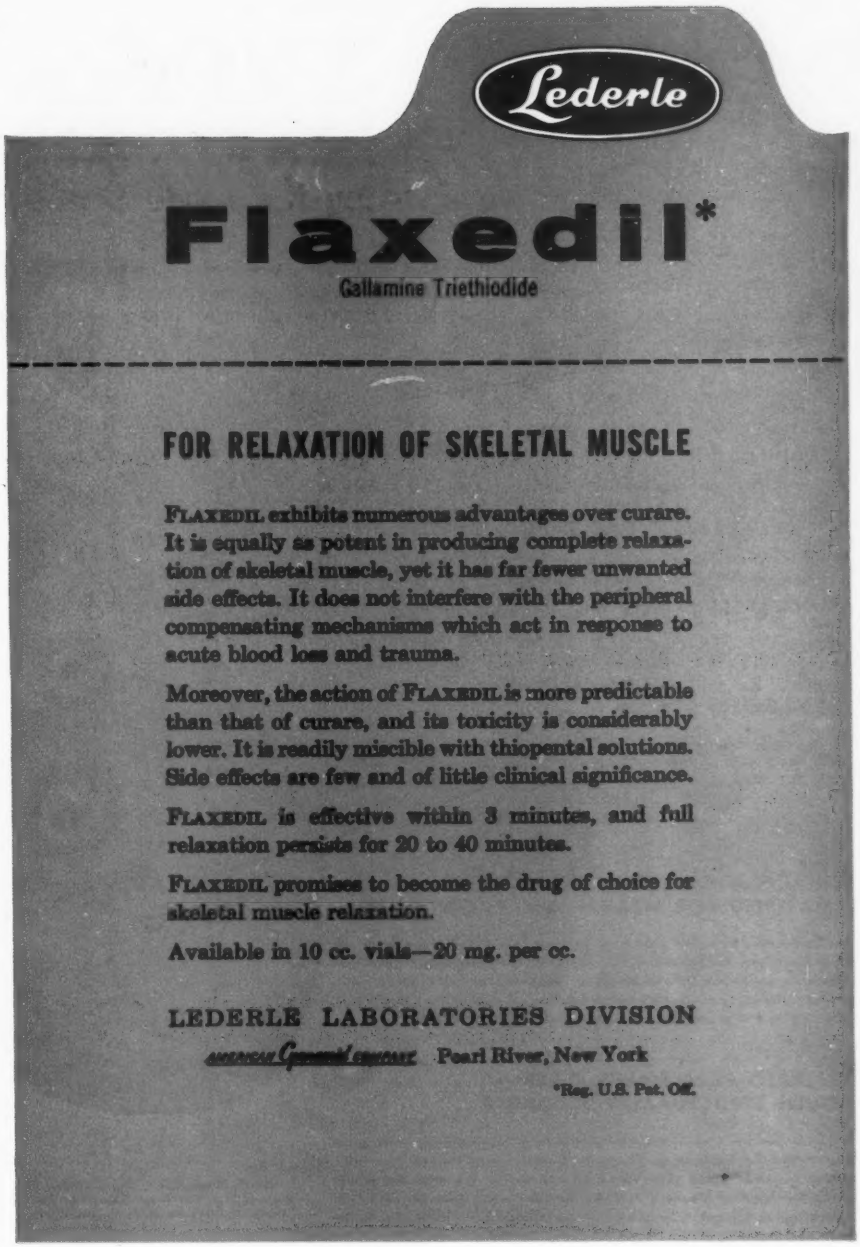
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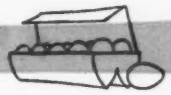

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Clinical Applications of Recent Research

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IN THE MALE

limacteric.[3]

ervousness, fatigability, insomnia, and de-
ession as well as flushes, sweats, and palpi-
ions are common in the male climacteric.
uscle tone, strength, libido, and potency
crease as the condition continues. Recog-
ion of this syndrome may be facilitated
means of a "therapeutic test" with an-
ogen. Male climacteric symptoms may be controlled completely with ORETON therapy.

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IN THE FEMALE

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emenstrual Tension.[5,6]

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sterone gives "singularly excellent re-
lts...."[5] This regimen retains efficacy month
er month without toxicity, gastrointesti-
upsets, or alterations in the cycle. Methyl-
tosterone is given orally, 10 mg. three
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th day of a 28 day cycle. Adjustment is
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recent advance is the combined adminis-
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BLIOGRAPHY (1) Lisser, H., and others: Postgrad. 8:39-, 1950. (2) Salmon, U. J., in Meigs, J. V., and Sturgis, .: Progress in Gynecology, New York, Grune & Stratton, vol. 2, p. 284. (3) Goldzieher, M. A., and Goldzieher, : Geriatrics *8*:1, 1953. (4) Sohval, A. R., in Soffer, L. J.: Diseases of the Endocrine Glands, Philadelphia, Lea & Febiger, 1951, p. 454. (5) Kupperman, H. S., and Goodman, S. J.: Am. J. Obst. & Gynec. *65*:141, 1953. (6) Kupperman, H. S., and Studdiford, W. E.: Postgrad. Med. *14*:410, 1953. (7) Preston, S. N., and Campbell, H. B.: Obst. & Gynec. *2*:152, 1953.

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Clinical Application of Recent Research

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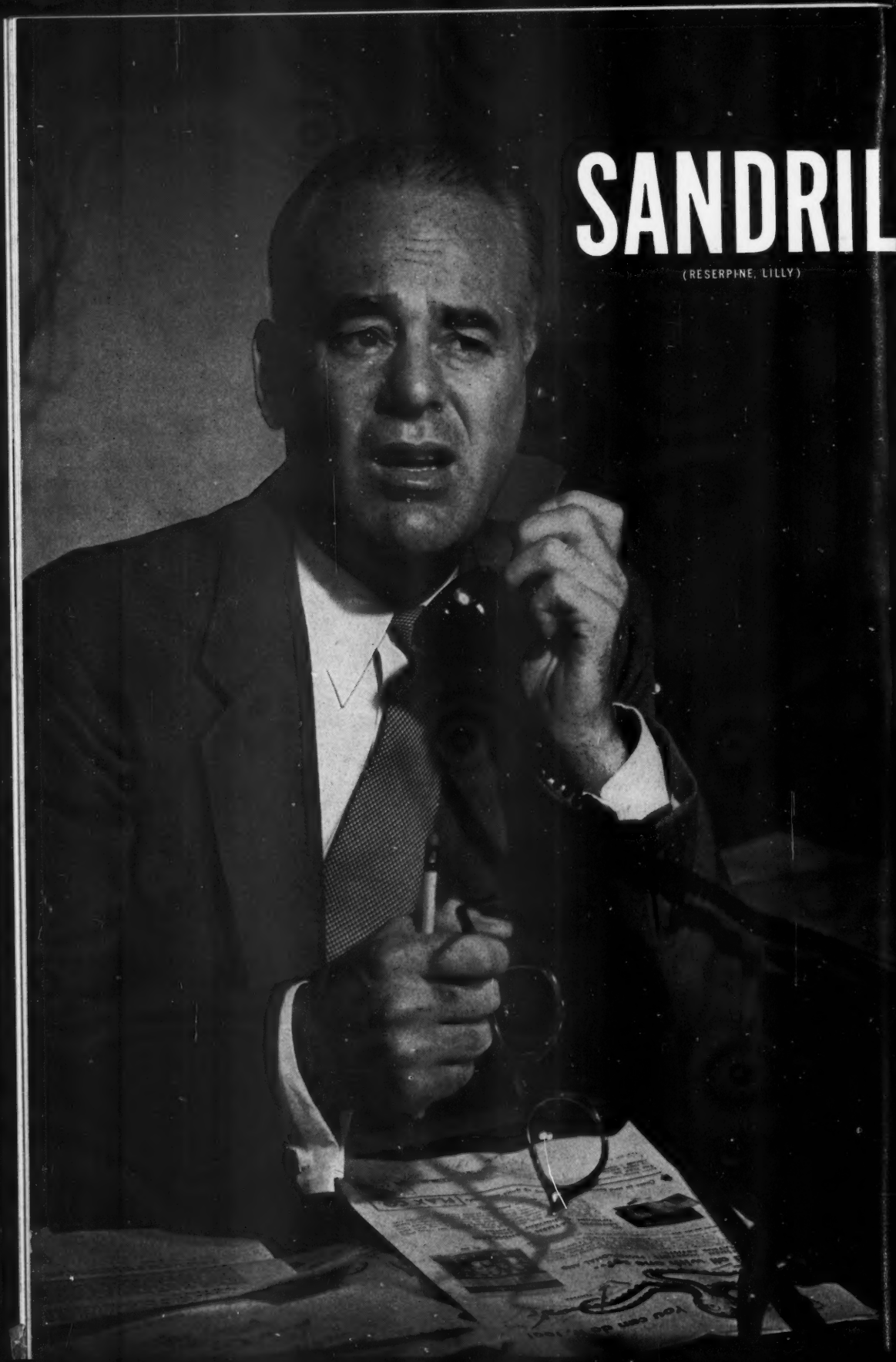
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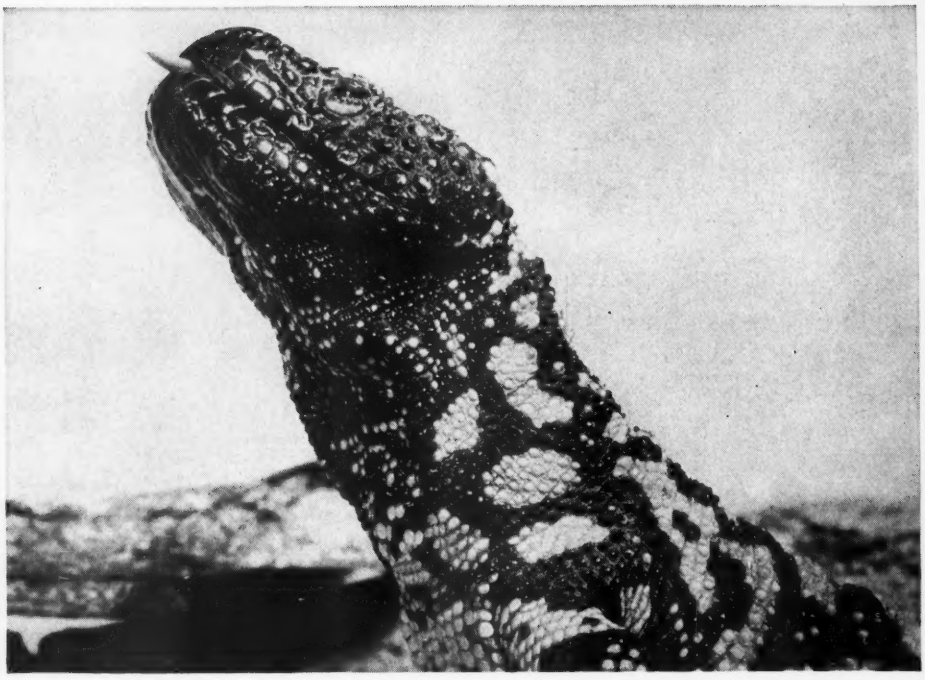

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Hammarlund, E. R., and Rising, L. W.: J. Am. Pharm. A. (Scient. Ed.) 41:296, 1952.

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1. Hankins, J. R., and Yeager, G. H.: J.A.M.A. 155:1306 (Aug. 7) 1954

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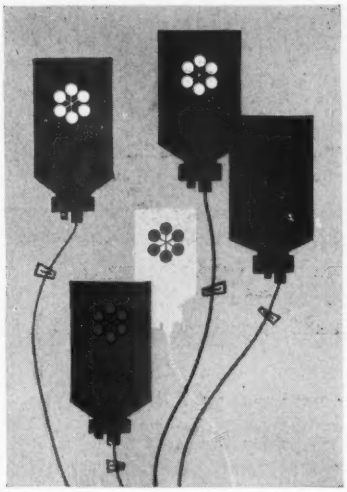

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1. Taggert, H. A.: Pennsylvania M. J. 54: 330, 1951.

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therapeutically	particularly valuable in general oozing fully compatible with vitamin K
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Joseph, M.: Am. J. Surg. *87*:905, 1954

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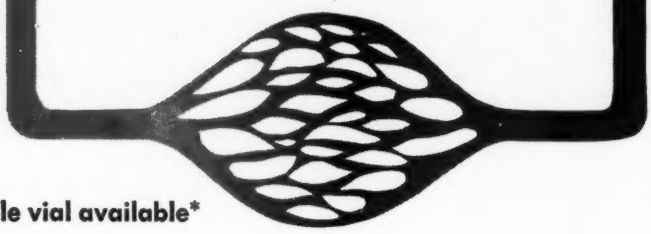

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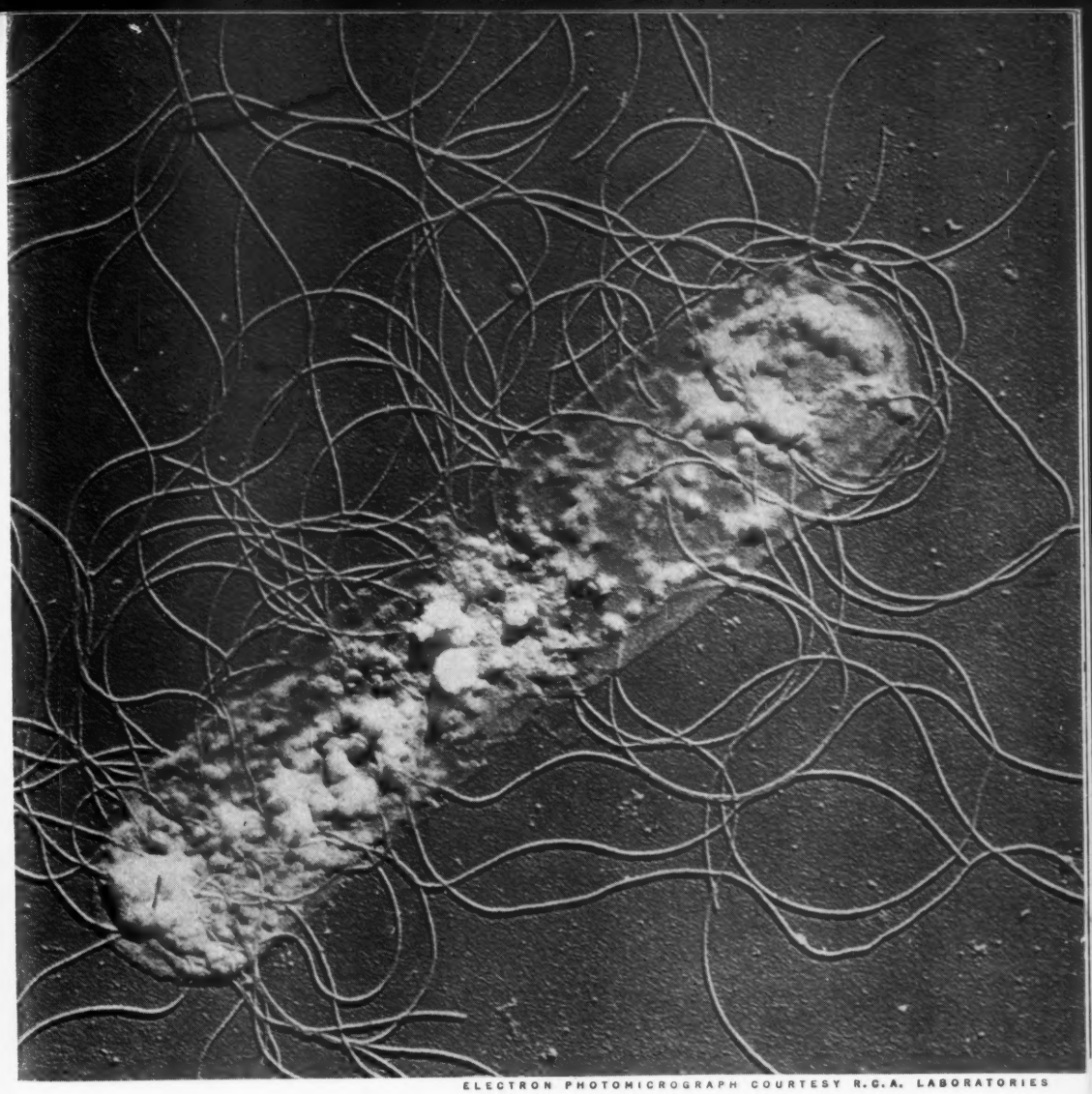

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*Bibliography of 192 references available on request.

1. Holly, R. G.: The Value of Iron Therapy in Pregnancy, Journal-Lancet 74:211 (June) 1954.
2. Kato, K.: Iron Cobalt Treatment of Physiologic and Nutritional Anemia in Infants, J. Pediat., 11:385 (Sept.) 1937.
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4. Weissbecker, L.: Cobalt Therapy, Dtsch. M. Wschr., 75:116 (1950).
5. Coles, B. L., and James, U.: The Effect of Cobalt and Iron Salts on the Anaemia of Prematurity, Arch. Disease in Childhood 29:85 (1954).
6. Quilligan, J. J., Jr.: Effect of a Cobalt-Iron Mixture on the Anemia of Prematurity, Texas St. J. Med. 50:294 (May) 1954.

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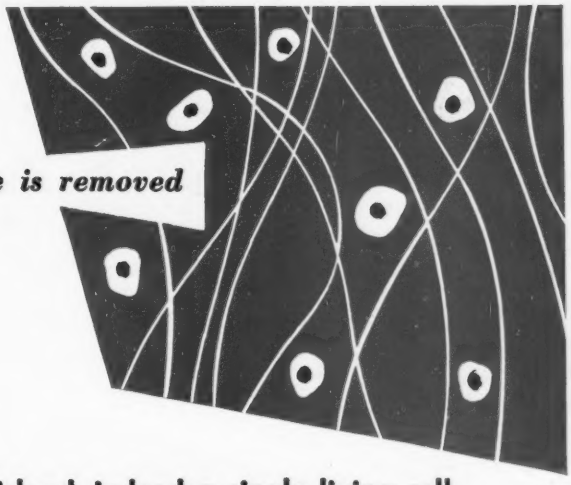

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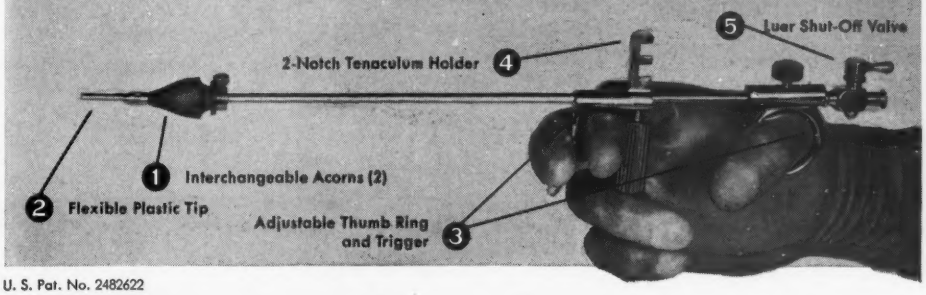
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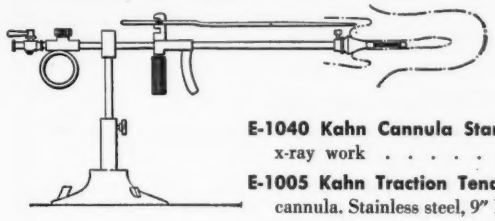

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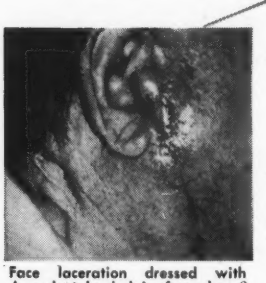

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1. Rigler, S. P. and Adams, W. E.: Experience with a new sprayable plastic as a dressing for operative wounds, Surg. 36:792 (Oct.) 1954. (University of Chicago Clinics, Chicago, Surgical Service).

2. Choy, D. S. J.: Clinical trials of a new plastic dressing for burns and surgical wounds, Arch. Surg. 68:33 (Jan.) 1954. (Bellevue Hospital, New York, Third Surgical Division—Dr. John Mulholland, chief).

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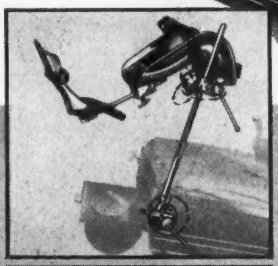

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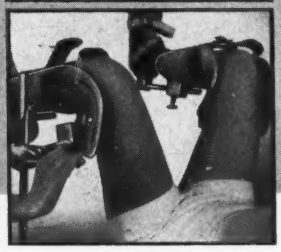

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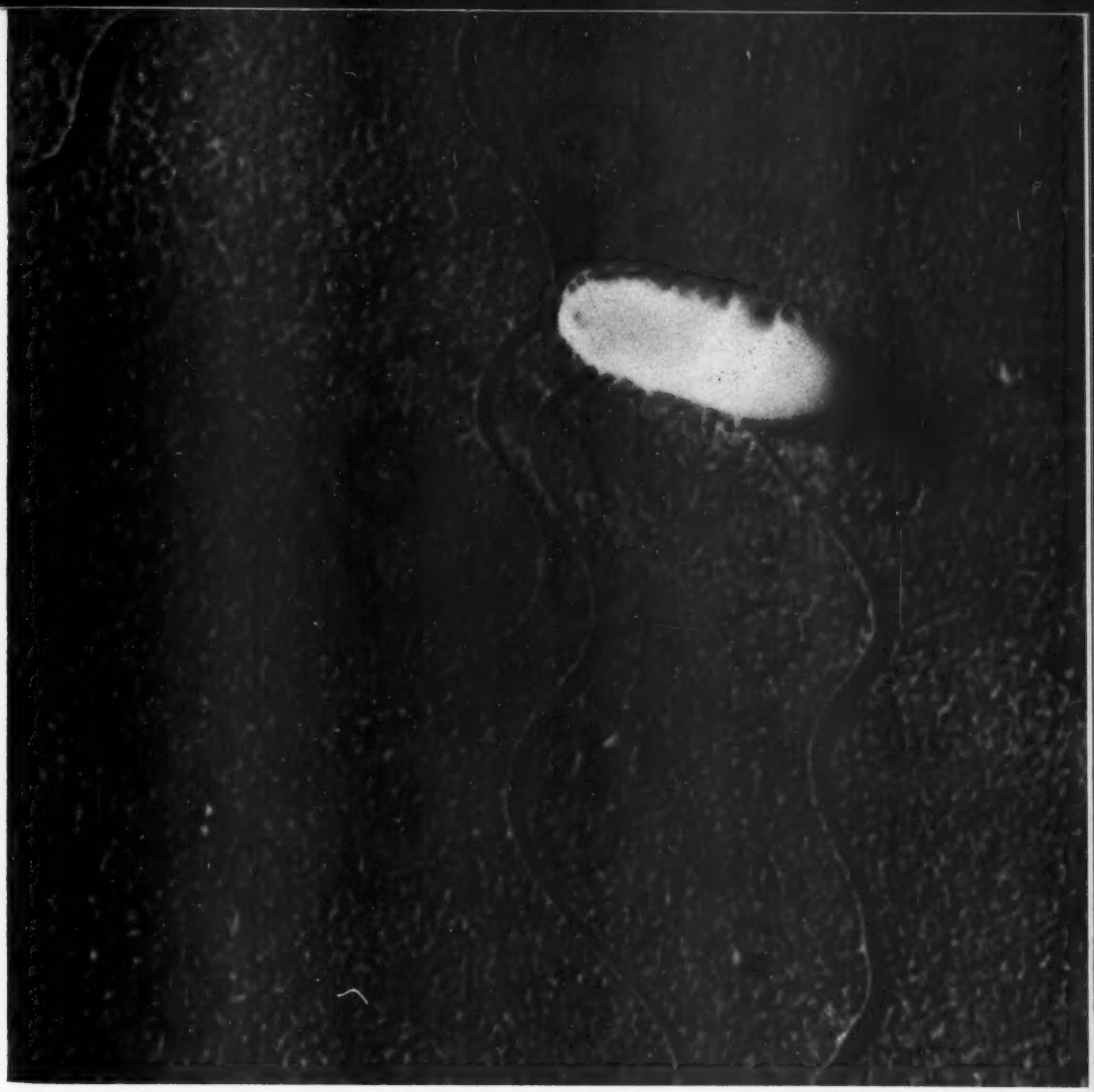

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It is another of the more than 30 organisms susceptible to

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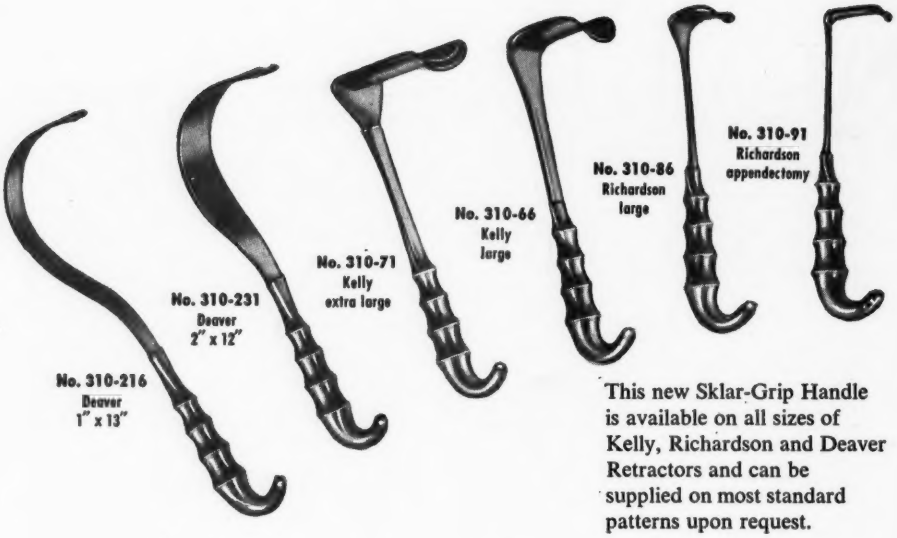

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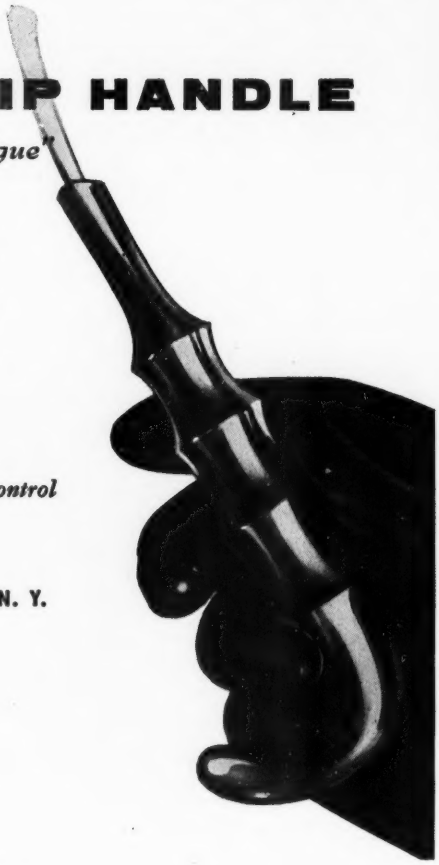

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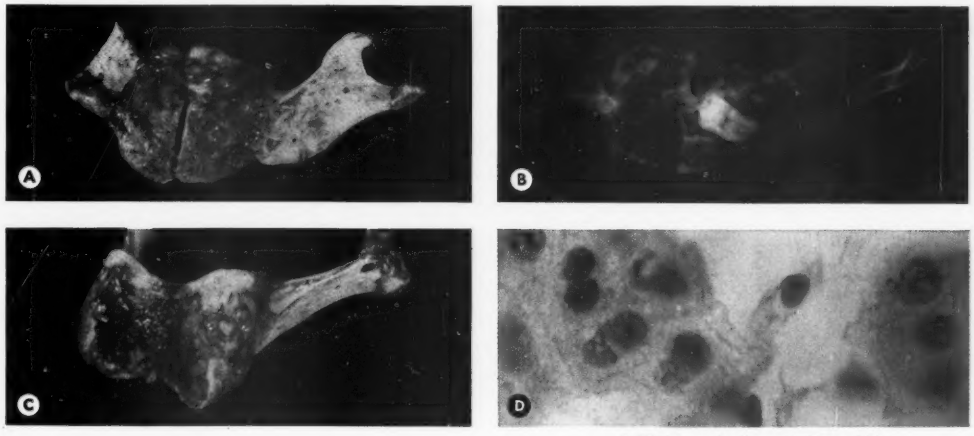

A. Photograph of resected mandible.

B. Radiograph of resected mandible.

C. Photograph of resected mandible cut to show appearance of cross section.

D. Photomicrograph (×1000) of resected mandible.

The radiographs and color photographs reproduced on this and the following page illustrate a mandibular resection. Better than hundreds of words, they show how radiography and photography work, day in and day out, to aid physicians and students in diagnosis, teaching, and research.

Radiographs and photographs: Veterans Administration Hospital, Bronx, New York.

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Postoperative posteroanterior and lateral oblique radiographs showing restoration of mandible with acrylic (radiolucent)

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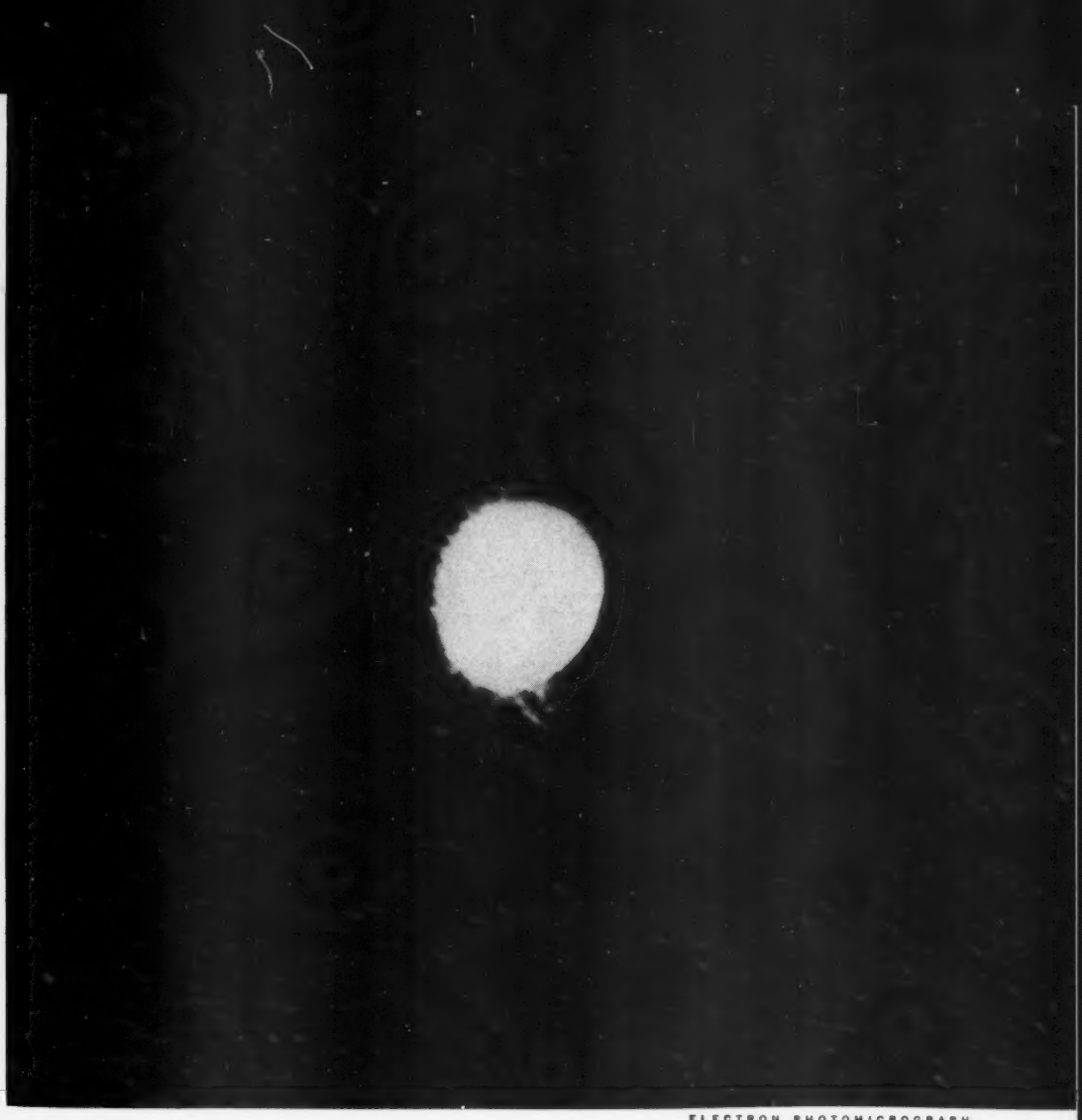

ELECTRON PHOTOMICROGRAPH

Staphylococcus aureus 35,000 X

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1. Thorn, G. W., *et al.*, *New England J. Med.* **248**:632, April 9, 1953.

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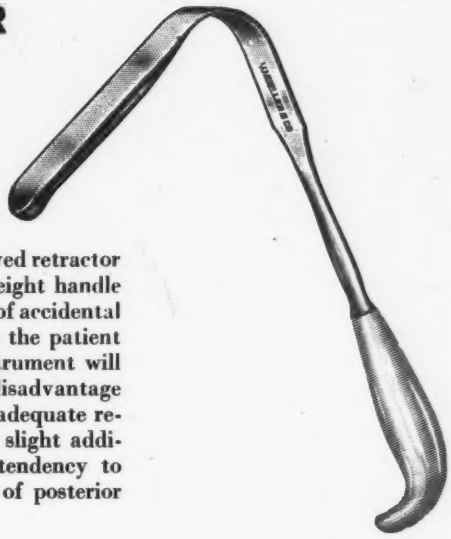
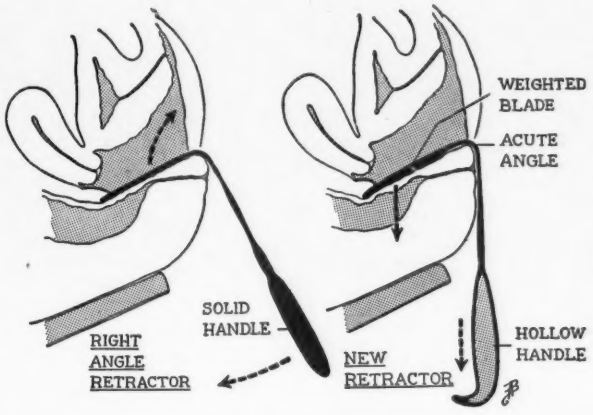


The long, weighted blade (5″x1″) of this improved retractor is at an acute angle on its extremely light weight handle to provide downward pressure with no danger of accidental dislodgment from the cul-de-sac. Even when the patient is placed in Trendelenburg position, this instrument will not fall out of place, thus overcoming a major disadvantage of other retractors. In addition to the quite adequate retraction afforded by the weighted blade, the slight additional pressure it provides has a welcome tendency to diminish bleeding—particularly the amount of posterior cuff vascular oozing.



The sketches at left, by direct comparison, show the advantages of the improved instrument. As gravity swings the weighted handle of the usual retractor toward the vertical, even if care is used the instrument has a tendency to fall out. The longer, weighted blade of the Glenner retractor provides a pull directly downward; the acute angle permits the handle to hang vertically, yet prevents the retractor from falling out when touched.

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REFERENCE: The American Journal of Obstetrics and Gynecology, Volume 67, Number 1; pp. 208-209.

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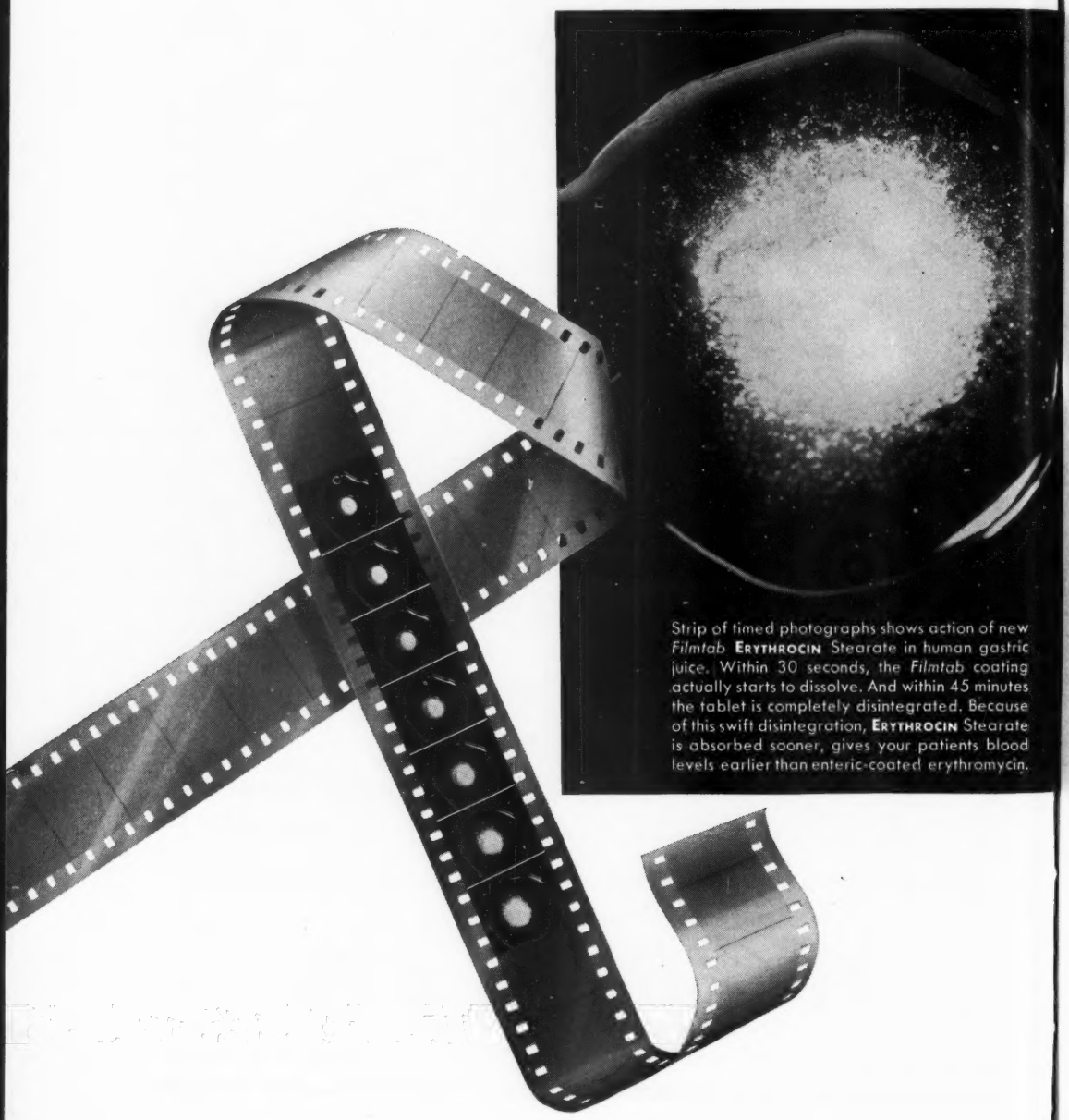

Strip of timed photographs shows action of new *Filmtab* **ERYTHROCIN** Stearate in human gastric juice. Within 30 seconds, the *Filmtab* coating actually starts to dissolve. And within 45 minutes the tablet is completely disintegrated. Because of this swift disintegration, **ERYTHROCIN** Stearate is absorbed sooner, gives your patients blood levels earlier than enteric-coated erythromycin.

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disintegrates faster than enteric-coated erythromycin

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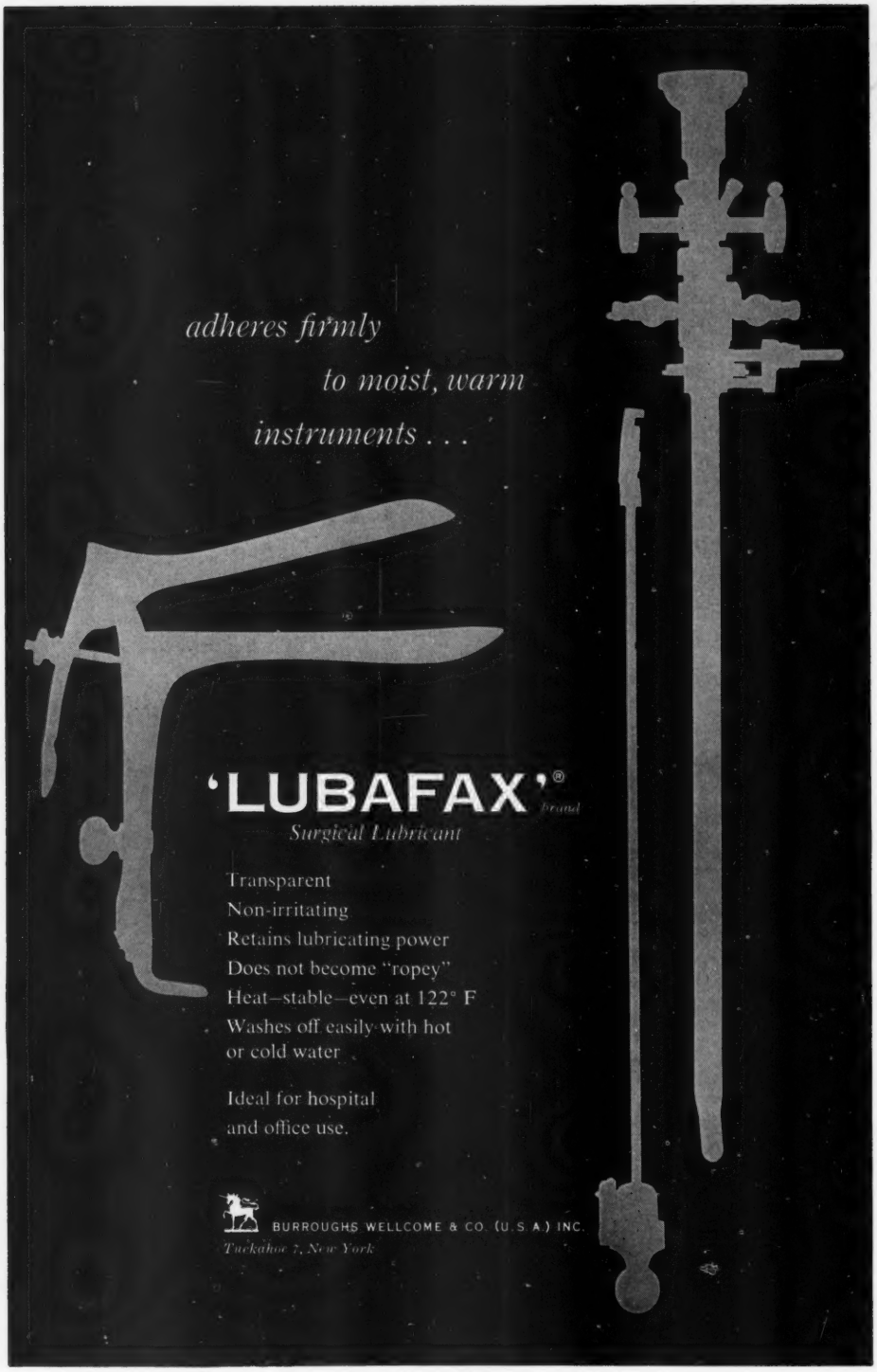
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Pantothenic Acid ..... 5 mg.
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Rice Bran Extract ..... 1 Gm.
Inositol ..... 30 mg.
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(Equiv. to 25 mg. of elemental iron)
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1. Grayzel, H. G., Heimer, C. B., and Grayzel, R. W.: New York St. J. M. 53:2233, 1953.
2. Heimer, C. B., Grayzel, H. G., and Kramer, B.: Archives of Pediatrics 68:382, 1951.
3. Behrman, H. T., Combes, F. C., Bobroff, A., and Leviticus, R.: Ind. Med. & Surgery 18:512, 1949.
4. Turell, R.: New York St. J. M. 50:2282, 1950.

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1. Garrett, T. A.: Personal communication.

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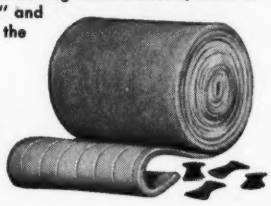

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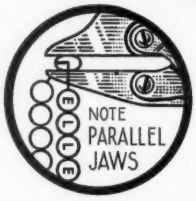

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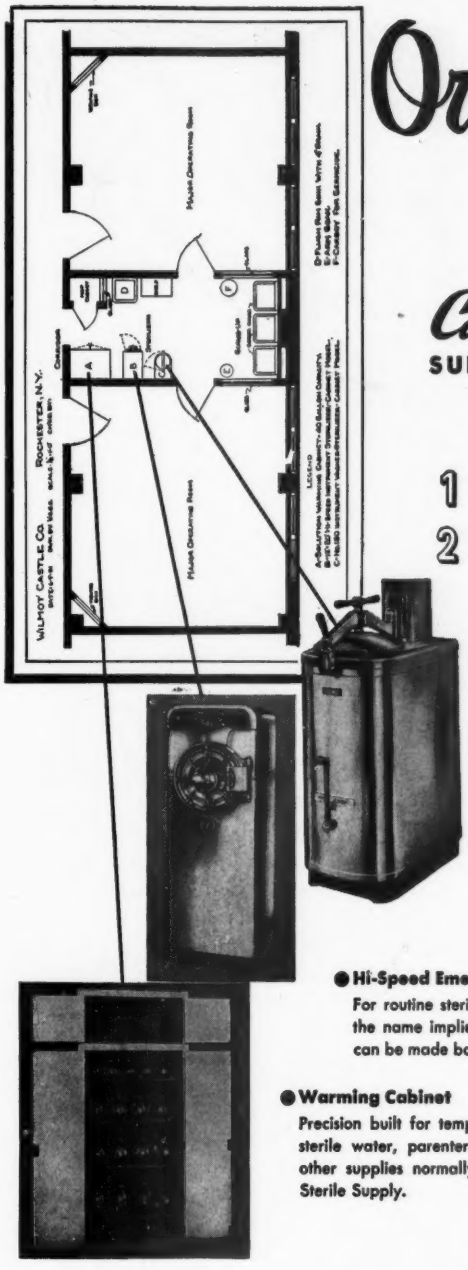

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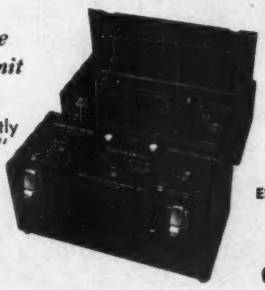

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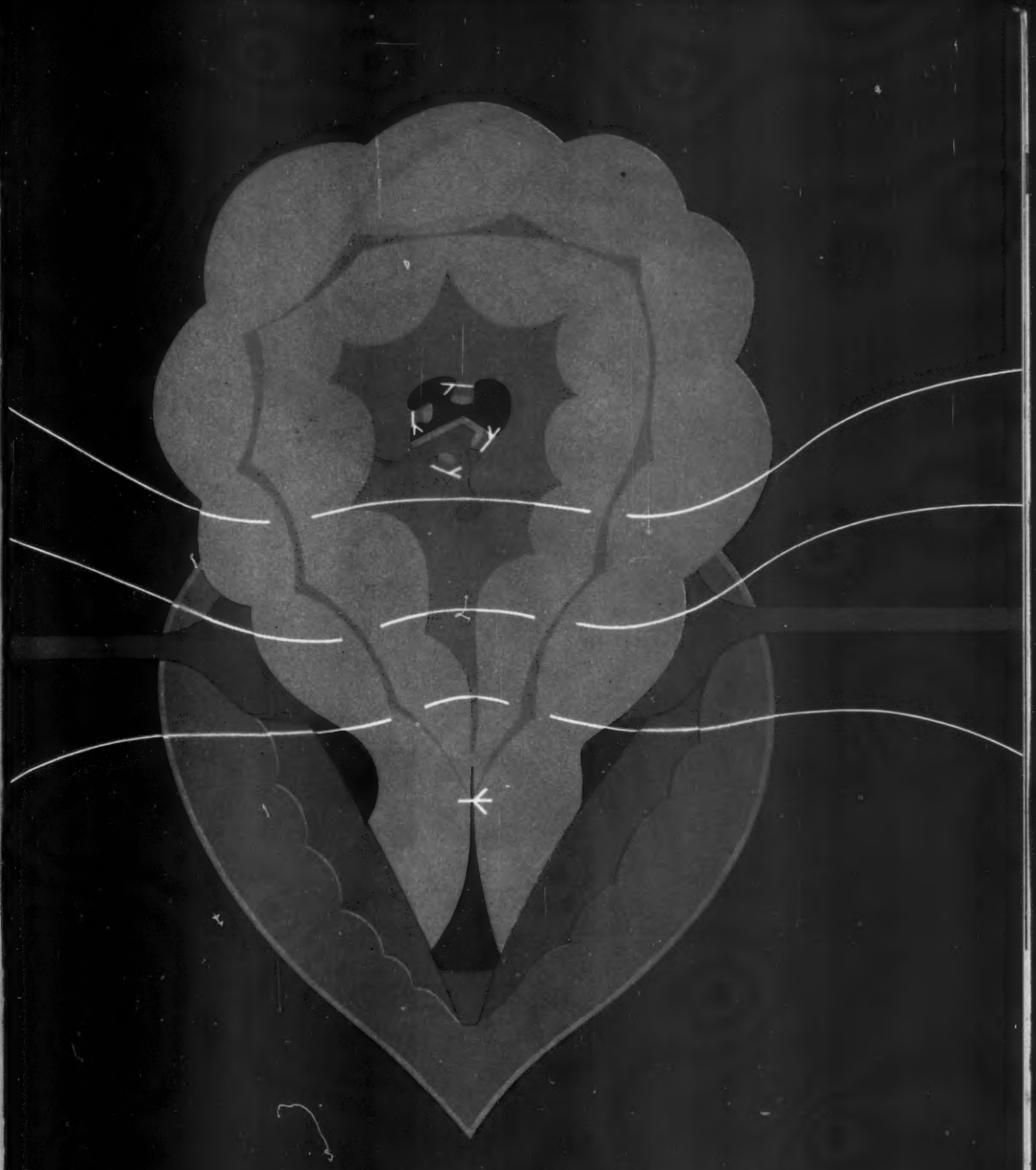

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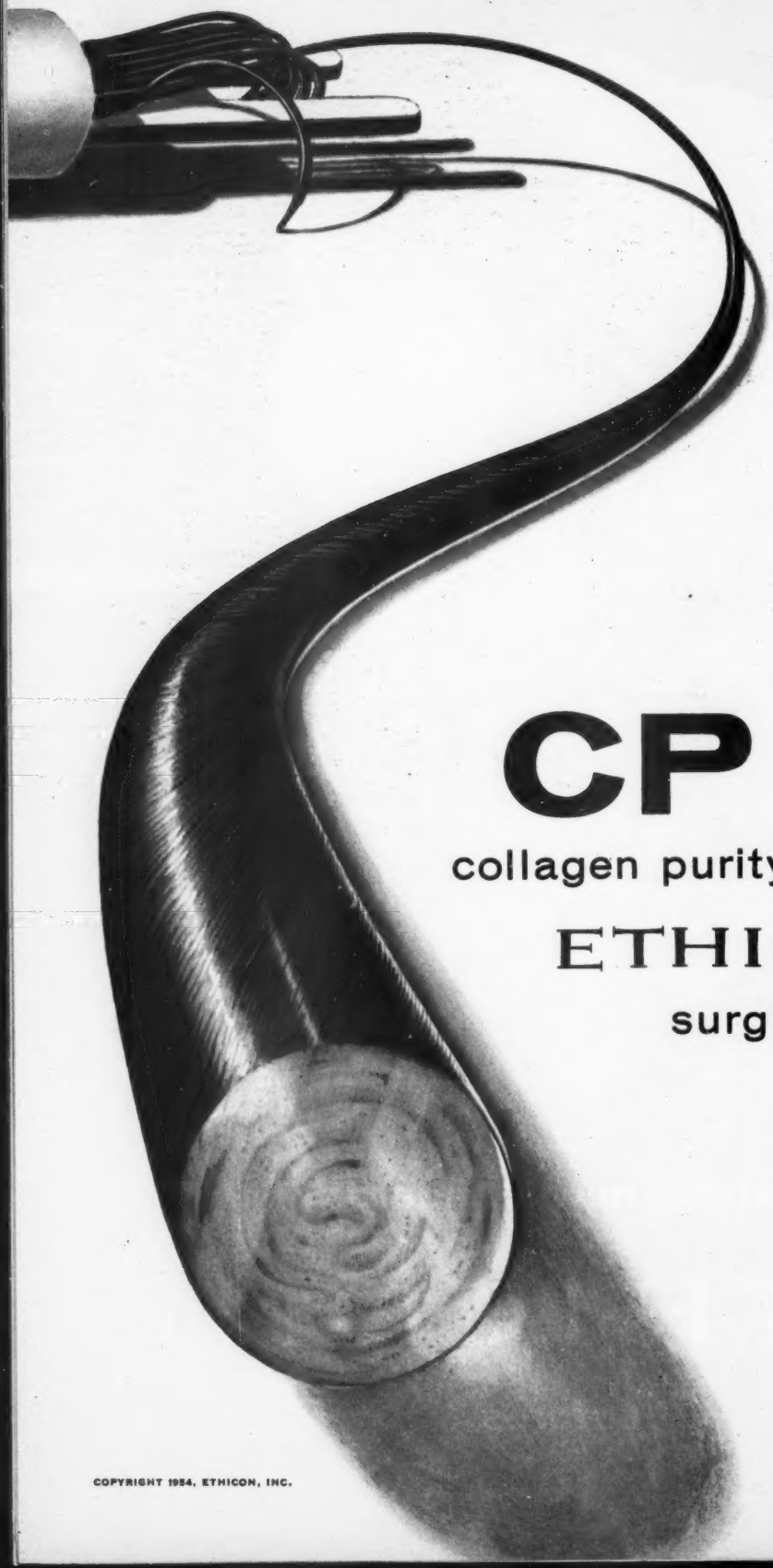

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1. Lancet **1**: 490, March 6, 1954.

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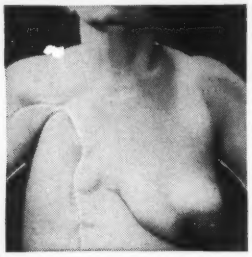

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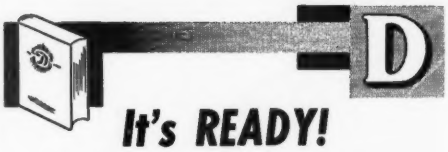

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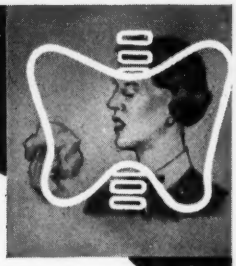

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Cheney, M. C.: GP 10: 32 (July) 1954.

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1. Beling, C. A., et al.: *Geriatrics 7:179 (May-June) 1952. 2. Barbour, C. M., Jr., and Tennant, R.: J. Urol. 71:497 (April) 1954. 3. Reich, C., and Wagner, E. J.: New York State J. Med. 50:1833 (Aug. 1) 1950. 4. Parsons, W. H.,* et al.: *Ann. Surg. 135:791 (June) 1952.*

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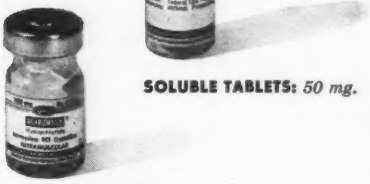

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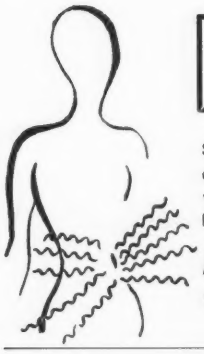

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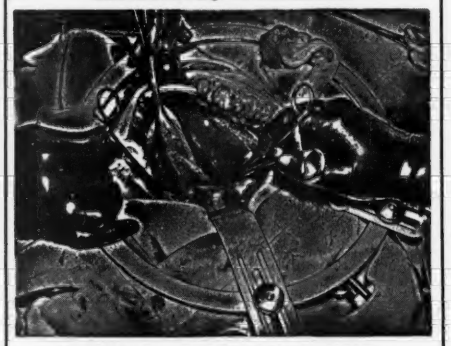

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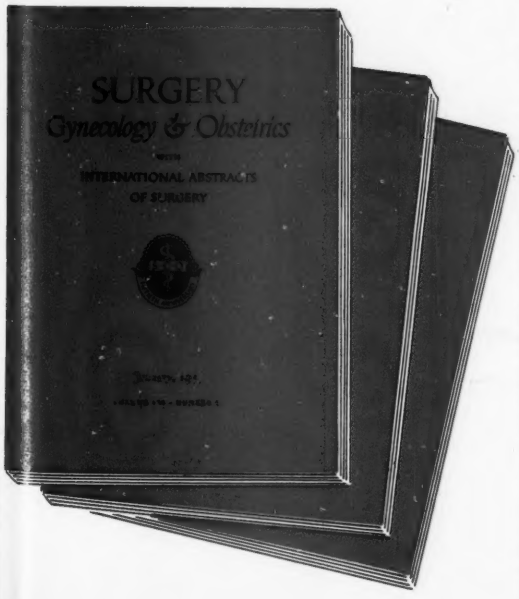

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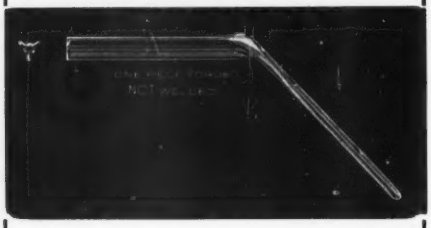

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